Special Number devoted to Rickets, Osteomalacia and Osteofibrosis.

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APRIL, 1934.

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APRIL, 1934.

Editorial

SKELETAL DISEASES OF DOMESTICATED ANIMALS.

THE articles which we publish in this issue of the Journal formed the subject of three lectures on the osteodystrophic diseases of domesticated animals given by Sir Arnold Theiler about a year ago under the auspices of London University, and delivered at the Royal Veterinary College in London.

They deal with problems which have been, and still are, of great economic importance in many parts of the world, including the British Dominions oversea. South Africa offered exceptional opportunity for the study of some of the diseases concerned, and Sir Arnold Theiler, then Director of Veterinary Research in the Union, together with Dr. P. J. du Toit, his present successor, and Dr. H. H. Green, at that time sub-director in charge of the biochemical department at Onderstepoort, undertook extensive investigations into the ætiology of the naturally occurring disease " stijfsiekte " and into the fundamental aspects of mineral nutrition of ruminants. Amongst the papers published by these workers was one —" Minimum Mineral Requirements of Cattle "—which recorded experiments designed to reproduce the naturally occurring "stijfsiekte," and throw particular light upon bovine metabolism in relation to the elements calcium and phosphorus. The material from these experiments was subsequently worked up by Sir Arnold Theiler from the histo-pathological point of view, an aspect which has been somewhat neglected in considering skeletal diseases in veterinary pathology. Through his microscopic studies he has been able to bring the bovine diseases into line with diseases described in human pathology, and to show that the naturally-occurring " stijfsiekte " and the experimentally-produced " aphosphorosis "

are typical " rickets " in young bovines and " osteomalacia " in older animals; names which have been somewhat loosely used in veterinary literature in the past, but which the author uses in their precise histo-pathological sense.

Sir Arnold then extended his investigations into skeletal diseases of equines, and, using material supplied by Sturgess and Crawford from Ceylon as well as material collected by himself from South Africa, has been able to confirm the view that the disease commonly described as " equine osteomalacia " by some authors and " osteoporosis " by others, is not osteomalacia as defined by human pathologists, but is a different pathological entity, more comparable to the " ostitis fibrosa " of man. It is properly termed " osteodystrophia fibrosa." Within the last seven years this disease of equines has formed the subject of experimental research in Ceylon, Japan and the Philippine Islands, and, as shown in the third lecture, its ætiology is now established.

The various investigators have shown that mineral deficiencies are the cause of the most important skeletal diseases of cattle, sheep and horses. Phosphorus deficiency leads to rickets and osteomalacia in cattle, and excess of phosphorus in relation to inadequate calcium leads to osteofibrosis in equines. The signification of mineral imbalance, however, is not the same for all species of animals, thus showing a difference in their physiological reactions. A ration which produces osteodystrophia fibrosa in the horse does not necessarily produce that disease in cattle. Indeed, that disease is apparently unknown in the bovine. In the case of the dog, the diseases rickets and osteomalacia do not naturally arise from the same cause as in cattle. The physiological needs of the dog and the conditions under which it lives in the domesticated state are such that deficiency of vitamin D probably plays the most important rôle. Sir Arnold has made it clear that the same pathological entity can have a different ætiology in different domesticated animals, and that the same ætiological conditions may give rise to pathologically diverse disorders. The material presented in the lectures is of great importance, and should assist in the interpretation of skeletal changes in various species of animals, even when the causal factors are still unknown. The work is not only of fundamental theoretical interest, but is of very great practical economic importance as indicating directions for prevention and cure of the diseases discussed. The lectures should assist in clearing up existing confusions in classification, establish definite ideas in an obscure subject, and point the way to further researches in an important field of veterinary science.

General Articles

THE OSTEODYSTROPHIC DISEASES OF DOMESTICATED ANIMALS.

By SIR ARNOLD THEILER, K.C.M.G., Hon. Assoc. R.C.V.S.

(1) The Structure of the Bone; Atrophy; Osteoporosis; Osteomyelitis.

DISEASES affecting the skeleton as a whole have been described in the veterinary literature under various names, and conceptions of their nature have varied widely. Even to-day the names in common use do not always reflect the real character of the disease, and the same name is sometimes used for pathologically diverse disorders. The clinical aspect of skeletal diseases of domesticated animals always received close attention, since the effects were generally so manifest that even the less experienced observers could not miss them; but until fairly recently we knew little of the morbid lesions beyond the pronounced changes obvious to the naked eye, *e.g.*, increase in size of certain bones, or reduction of weight, or porosity, or increased fragility or flexibility. Concerning the cause of the changes there was very little unanimity of opinion, and the general tendency was to bring the ætiology into line with that of diseases of the same name in man.

The tendency in veterinary pathology to conform ideas and terminology to those prevailing in human pathology is natural enough, and should indeed be encouraged, since the same fundamental principles are applicable to animals and man. But great care has to be exercised in the interpretation of borrowed terms. Where veterinary pathology has sometimes gone wrong has been in applying names used in human pathology to diseases of animals on grounds of gross clinical or macroscopic similarity, without comparing histological details. In reading the earlier veterinary literature, one cannot get away from the impression that, once the name of a disease had been transferred from man to an animal, most of the ideas of causation went over as well, without sufficient scrutiny of the evidence available for alternative explanations. This has led to a great deal of misunderstanding, particularly in regard to the diseases I propose to discuss.

The primary principle in the definition of a disease should be its ætiology, and diseases of different species of animals should be treated as the same if they have the same cause, notwithstanding considerable differences in clinical aspects and in morbid anatomy. Unfortunately, however, the ætiological principle cannot be applied to the differentiation and identification of the various osteodystrophic diseases of different species of animals, because even yet we do not know all the causes which produce them. Although recent experimental research into deficiency diseases promises to supply us with a starting point, we have at

present still to fall back upon the histogenetic principle, according to which tissue changes form the basis of classification and comparison.

The osteodystrophic diseases which I propose to consider are known in the older English veterinary literature under the names of rickets, osteomalacia and osteoporosis. The name rickets was generally applied to a condition found in young animals; osteomalacia and osteoporosis to one found in older animals. In French terminology the terms " rachitisme " and " ostéomalacie " are used in a similar sense, although by some authors the latter word is replaced by the term "cachexie osseuse." In the German literature the equivalent terms are "Rachitis" and "Osteomalazie." The term osteoporosis has been used to describe a pathological condition prominent in generalised diseases of the skeleton; but it has also been used to denote a specific disease or definite morbid entity.

These diseases have been, and still are, of great economic importance in various parts of the world. They interested me from the ætiological standpoint since the days of my earliest veterinary activities in South Africa, and more recently I have taken up their study from the histo-pathological point of view. The opportunities for observing some of the diseases, notably bovine osteomalacia, were exceptionally good in that sub-Continent, and a considerable amount of clinical evidence was collected. Thanks to the well-equipped laboratories at Onderstepoort, experimental work by myself and my colleagues became possible on a comprehensive scale, and this did much to solve problems of ætiology and to provide material for histological examination. The result of the Onderstepoort researches forms the basis of my present discussion, and I shall compare my deductions with those published by other authors. But before doing so it is advisable first to discuss the structure and physiology of normal bone, so as to set forth a clear conception of observed pathological changes and to be able to interpret their meaning. My own study of the architecture of bone has led me to certain conceptions which, in my opinion, are not sufficiently emphasised in text-books, and I will try to include them in my presentation. According to their phylogenetic and ontogenetic origin, two types of bone are distinguished: those of membranous and those of cartilaginous origin. The former are found in certain parts of the skull, while the latter build up the skeleton of the body. In the latter, cartilage forms a temporary model for the bone, and acts as the primary support for the deposition of the osseous tissue which gradually replaces it as the animal develops. This deposition of osseous tissue begins as an osseous focus in definite positions in the cartilaginous model, and we distinguish bones with one focus, or with two or three foci. The growth of these foci gradually replaces the cartilage, which finally vanishes, except in those parts of the bone which are transformed into articulations. During the early period of life, the so-called juvenile age, intermediary cartilage persists in definite localities, separating the epiphyses from the diaphyses, and forms a centre of growth by which longitudinal extension of the bone can occur. Once the proliferation of cartilage cells is arrested, further extension ceases, and final ossification follows. Certain inter-

mediary cartilages disappear sooner than others, and the period of ossification varies in different animals. In man it takes place at a comparatively late age, and it is important to remember this in comparing bone lesions in the human subject with those in animals which complete ossification at an earlier stage of life. It is of practical importance to know at which age the different epiphyseal lines disappear in various species of animals. These centres of growth play an important rôle in the pathology of the skeleton, since they become affected in various ways, and each type of alteration has its own significance from a differential diagnostic point of view. At the beginning of its conversion into tela ossea the cartilaginous model is invaded by blood vessels, which originate in the periosteum and carry connective tissue along with them. The latter forms the supporting fibrillar network of the hematopoietic or lymphoid marrow, an independent tissue, which has nothing to do with the ordinary function of bone, and which in the longitudinal bones is soon replaced by an adipose tissue or fatty marrow. The invading connective tissue also forms the endosteum, and its cells adopt the specific function of forming lamellar substance, being then termed osteoblasts. The blood vessels with their envelopes advance into the cartilage, reducing it to fragments, upon which the osteoblasts deposit lamellar osseous substance forming the cancellated tissue or spongiosa. The cartilage is gradually withdrawn into the ends of the diaphysis, leaving behind the already-mentioned intermediary cartilages or epiphyseal lines, of which one or two occur, according to the type and position of the bone. This intermediary cartilage continues to proliferate during the period of growth of the animal, and the deposition of osseous substance conforms to a definite pattern. The epiphyseal line shows different zones of activity. The zone nearest the epiphysis consists of dormant or resting cells which go over into proliferating cells arranged in parallel columns, and which finally hypertrophy. The intervening ground substance of the hypertrophic zone calcifies, forming the so-called "provisional zone of calcification." The vessels of the bone marrow, with their supporting tissue, follow the cellular columns in the form of primary medullary canals, breaking down the cartilaginous tissue and depositing osteoid lamellar substance on the walls of the septa. The osteoid then becomes calcified, and is thus converted into proper tela ossea. Certain septa in the adjacent subchondral zone are not resorbed, but act as connective pillars to the spongiosa, forming the first support for the trabeculæ, which in due course make up the cancellated tissue. Simultaneously with the entrance of periosteal connective tissue into the cartilaginous model, the formation of periosteal bone begins, a differently organised tissue, which is intended to form the compacta. This is responsible for the peripheral growth or increase in thickness of bone. In the formation of periosteal osseus tissue a prominent part is played by the connective tissue, which undergoes active cellular proliferation and produces osteoblasts to deposit osteoid in the fibrous tissue. At the same time definite canalisation goes on in the adjacent tissue, leaving a framework which is duly lined with lamellar tissue. The structure formed has a regular pattern, which in longitudinal and cross sections of the diaphysis looks lamellated, but

which can be shown to consist of tubes arranged in three-spatial directions and imbedded in calcified fibrous tissue. In any tube of the three-dimensional lace-work three different portions can be recognised: an outer one, containing the conspicuous original fibrillæ of the periost; an intermediary one with remnants of the original fibrillar periost and with lamellar substance deposited between the fibrillæ; and an inner one consisting entirely of lamellar substance lining the tube. A longitudinal section of such a tube thus appears as a lamella bordered on both sides by a strip of tissue of fibrous origin and with a canal in its centre. From these strips fibrillæ, the so-called Sharpey fibres, enter the lamellar substance, but do not reach the central portion. Sharpey fibres are thus characteristic for bone of periosteal origin. Since fibrillar tissue and lamellar substance both take part in the construction of periosteal tubes, these should be distinguished from the true Haversian systems, which consist entirely of lamellar substance. They should be called mixed or periosteal systems. In the evolution of bone they only form a passing stage, and are gradually replaced by the final Haversian systems; the Haversian tubes being formed by deposition of lamellar substance on the walls of canals excavated in the preceding periosteal system. The implantation of these tubes begins around the medullary cavity, and they can be regarded as supporting elements in the structure, giving it a character like reinforced concrete. Apart from the main directions of development, these Haversian tubes also appear in places which seem to require additional strengthening. They are always separated from the tissue they replace by a delimiting line, which may be called the "cement line" ("Kittlinie" in German), and this feature is so characteristic that it helps to distinguish the Haversian tubes from the original periosteal ones of the mixed system. Fragments of the original mixed or periosteal systems are found lying between the Haversian tubes, often conferring a breccia-like aspect on the region as a whole. With advancing age the Haversian tubes invade the peri-osteal regions more and more, faster in some bones than in others, but always according to a definite plan. Generally speaking, the younger an animal is, the fewer Haversian tubes it has; whilst in an old animal they occupy practically the whole compacta of the diaphyses. In the compacta of the diaphysis of a normally growing bone, as, for example, in a bovine or equine about three years old, three different zones can be distinguished: an outer one of periosteal or mixed systems enveloped by the periosteum; an intermediary one of Haversian tubes and periosteal fragments; and an inner one of lamellæ. These "internal lamellæ" form the lining of the medullary cavity, and are homologous with those lining the spaces of the cancellated tissue of the spongiosa. It may be added that the ossifi-cation of the membranous portion of the skull follows the same general principle as just described for the periosteum. In the region of the epiphysis the compacta or corticalis gradually thins out, and the medullary cavity is filled by cancellated tissue, the trabeculæ of which in the adult consist exclusively of lamellar bone. In the growing bone the trabeculæ are either formed in the epiphyseal cartilage, and are therefore of endochondral origin, or they are cut out of the peripheral periosteal systems, and are therefore of fibrous origin; but in due course all are

replaced by lamellar substance laid down according to the plan which guides the growth of the bone and final arrangement of the trabeculæ. In the periphery of the epiphyseal cartilage of a growing bone the periosteal systems are either lacking or are reduced to a mere strip of ossified fibrous tissue. The compacta is mainly made up of lamellar bone derived by filling out the medullary spaces of the cancellated tissue, and it therefore resembles Haversian bone. After the growth of a bone in length comes to a standstill, growth in thickness continues for a considerable time *via* the periosteum. The trabeculæ of the cancellated tissue follow certain definite directions which suggest mechanical contrivances built for specific purposes, *e.g.*, a crane. Observation of this fact attracted attention to the detailed architecture of bone, and it is now realised that although bone is such a hard and solid structure, it is by no means an organ exempt from change. Although the shape and general inner architecture of bones are primarily determined by heredity, they are also influenced by modifying external factors, and the fundamental conceptions of Roux concerning functional adaptations apply to bones just as they do to other organs. Roux laid down the generalisation that the volume of an organ increases with activity (hypertrophy), and decreases with inactivity (atrophy), and he distinguishes qualitative and quantitative functional adaptations. According to him, exercise supplies a trophic stimulus on the cells, enabling them to increase in size and number; conversely, the nutrition of the cells suffers from inactivity, and atrophic changes occur. In the case of the skeletal system, the stimuli result from pressure, traction and torsion; the mechanical function of the bone is to resist stresses and strains, and in so doing its specific cells are brought into action. But the static and dynamic functions of bone are not the only ones it has to perform, and a study of the pathology of the osteodystrophic diseases suggests that under certain circumstances they are not even the primary ones. The nutritonal function of bone as a reservoir of minerals comes into prominence, and the mechanical efficiency of the skeleton is sacrificed for the good of the organism as a whole.

The organic matter of bone, called "ossein," is impregnated with earthy salts, of which the chief is tricalcium phosphate; and these, incidentally, confer upon bone its strength. But the elements calcium and phosphorus are also necessary for the general physiological activities of the organism as a whole: they are scattered throughout the tissues, and play a leading rôle in the plasma, which bathes every cell of the body. Special nervous endocrine and enzymic processes control their destiny, and although the skeleton contains the major quantities, it does not necessarily need them most, but acts as a reservoir for these elements. About 78 per cent. of the total ash of a live ox, or about 83 per cent. of the mineral matter of its carcase, are present in the bones, but under pathological conditions half of this may be sacrificed before the animal succumbs. The composition of bone is variable in the sense that the ratio of organic matter to mineral matter may vary, but the composition of bone ash is nearly constant even in different species of animals. The main constituent is tricalcium phosphate; minor constituents are calcium carbonate and the phosphates, and car-

bonates of magnesium and other bases. In one of our own experiments, in which a heifer was fed on a ration containing more than enough calcium and phosphorus, and showed a dense compact skeleton, the long bones showed on chemical examination 64 per cent. of ash after removal of fat; of this ash, about 53.8 per cent. was CaO and 43.8 per cent. P_2O_5. The requirement of a young animal for minerals depends upon its rate of growth: during rapid growth the available mineral salts are used principally for building up the skeleton. Relatively little storage occurs, but as soon as growth abates the quantity required for maintenance is small, and a definite storage mechanism comes into operation. The period of growth varies in different species of animals and even for different bones. It is governed by the capacity for proliferation of the intermediate cartilages. Longitudinal growth is first arrested in the bones of the extremities, but continues elsewhere for a considerable period, whilst growth in thickness goes on for some time after epiphyseal growth has ceased. Reliable experimental data on the quantities of different minerals required for growth are very limited, although indirect calculations are often made. Calcium has received most attention, because in the past it has been considered to be the constituent most likely to be lacking; but as we shall see presently, an acalcicosis is not the mineral deficiency disease of greatest economic importance amongst the domesticated animals. Various estimates have been made for the dietary calcium requirements of an animal by various indirect methods. For example, if we take milk, the natural food of the young animal, as a guide, and assume that protein and minerals are required in the same ratio, we find that a young bovine of about 500 lb. weight consumes about 1 lb. of protein per day, which if derived from milk would carry about 0.8 oz. CaO. Calculating on a different basis, we can take lime as constituting about 2 per cent. of the bodyweight of a bullock, and estimate that a young bovine of 500 lb. weight, putting on about $2\frac{1}{2}$ lb. per day, would require about 2 per cent. of 40 oz., *i.e.*, about 0.8 oz. CaO, as before. The requirements of phosphorus could be estimated in the same way, in which case they would come out as roughly proportional to those of calcium. But such calculations are arbitrary, and do not necessarily tell us the truth. The argument from milk is a teleological one, and assumes that milk not only contains optimal proportions of calcium and phosphorus, but that the animal cannot do with anything less perfect; and the argument from analysis of carcases tells us what quantities have been stored rather than what quantities must be fed.

Direct observations upon the requirements of the bovine for growth and maintenance were made by myself, with my colleagues Green and du Toit, at Onderstepoort, and these led to conclusions not quite in line with preconceived ideas. The dietary requirements for calcium were found to be much lower than generally believed, and the physiological requirements for phosphorus to be much higher than those for calcium. In a heifer which increased in weight from 483 lb. to about 1,200 lb. in twenty-two months, the small quantity of 8.2 g. CaO per day produced an almost normal skeleton when P_2O_5 was optimal. On the other hand, when calcium was present in the ration in more than adequate

1482

FIG. 1.—Heifer 804. Normal; control. Food sufficient in CaO and P_2O_5. Radius. Compacta. Cross section. In the periphery is seen the concentric arrangement of the so-called periosteal lamellæ, described in the text as mixed periosteal systems. A lamella is bordered on each side by fibrous tissue, and includes in the centre a canal. The lamella is a longitudinal section of a tube, which is surrounded by fibrous bone. A portion of the middle or Haversian zone is seen in the lower end of the picture. Haversian tubes with clear-cut margins are penetrating into the outer zone. Mag. 39 ×.

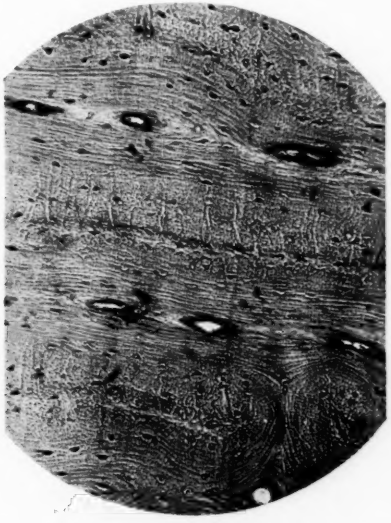

FIG. 2.—Heifer 804. Metatarsus. Compacta. Cross section. Two longitudinal sections of periosteal systems are seen under higher magnification. They are separated from each other by fibrous envelopes. The fibres appear to penetrate into the lamellar substance, which in fact has been deposited between them. The centre of the tube is occupied by the canal, which is lined by lamellar substance. The system is thus clearly composed of fibrous and lamellar substance. Mag. 152 ×.

148 b

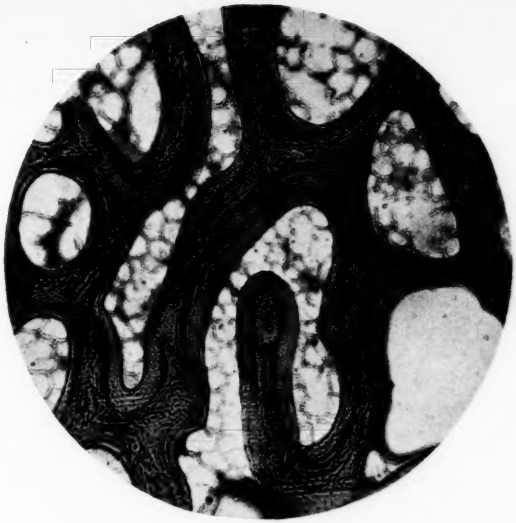

FIG. 3.—Heifer 804. Metatarsus. Distal epiphysis. Longitudinal section. Cancellated tissue. The medullary spaces are conspicuously lined with lamellar substance, representing stored minerals. The marrow consists of fat tissue. Mag. 39 ×.

FIG. 4.—Heifer 804. Tibia. Cross section. Lamellated lining of the medullary canal, bordering on the zone of Haversian systems, which have also been built into the outer periphery of the medullary or central zone. The lamellated zone represents the storage of minerals. Mag. 63 ×.

1480

FIG. 5.—Heifer 923. Food deficient in CaO. Metatarsus. Diaphysis. Cross section. The lamellated medullary zone has been eroded, and the medullary cavity encroaches on the zone of the Haversian systems. (Excentric atrophy). Mag. 39 ×.

FIG. 6.—Heifer 923. Food deficient in CaO. Third rib. Proximal end. The section is from the vicinity of the tuberculum costæ. Marked resorptive processes and thinning down of the trabeculæ. The marrow consists mainly of lymphoid cells and a few fat cells. Mag. 39 ×.

1484

FIG. 7.—Heifer 925. Suffering from an intercurrent osteomyelitis. Radius distal. Longitudinal section. Necrosis of the cartilage. Marked inflammatory infiltration of the metaphysis and formation of woven bone trabeculæ. Mag. 63 ×.

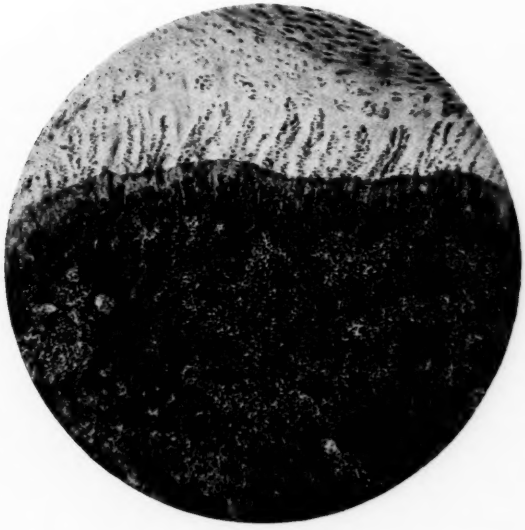

FIG. 8.—Heifer 923. Food deficient in CaO. Third rib distal. Longitudinal section. Normal arrangement of the cartilaginous cells, normal appearance of the provisional calcified zone, and normal process of ossification. Mag. 63 ×.

amount, a very much higher minimum of P_2O_5 was required. We concluded that, although about 10 g. CaO per day for slow growth or for maintenance at about 1,000 lb. liveweight would be a sufficient minimum for normal skeletal development, about 20 g. P_2O_5 would be needed, *i.e.*, for effective nutrition at the minimum physiological level about twice as much P_2O_5 as CaO would be required. This, of course, does not mean that a CaO : P_2O_5 ratio of 1 : 2 is a desirable one, but merely that the quantity of CaO can be cut down further than the minimum of P_2O_5 without producing disease. In the case of milk production, the requirements of both calcium and phosphorus naturally increase with the quantity of milk secreted; and the production of five gallons of milk per day—a not unusual yield from a good dairy cow at the height of lactation—involves a loss from the blood stream of about 39 g. CaO and 45 g. P_2O_5. The amount of calcium and phosphorus which have to be supplied in the ration to meet this drain depends upon the nature of the foodstuffs and the absorptive efficiency of the intestinal tract, but even on mineral-rich rations it may be difficult to meet lactation requirements. Metabolism experiments carried out by a number of observers have shown that on ordinary rations at the height of lactation a cow may pass into negative mineral balance, and lose more calcium and phosphorus in milk and excreta than it acquires in the food. From some of the experimental data it may be calculated that a cow can lose as much as 3½ lb. of calcium in twelve weeks. This would represent about 27 per cent. of the total bone calcium, and may therefore be assumed to be abnormal; but it serves to show the extent to which the skeleton can serve as a reserve for minerals required for other physiological purposes without the animal showing clinical signs of disease.

The concentration of calcium and inorganic phosphorus in the blood is much smaller than in the milk, only about one-twelfth as high, and is normally kept at a fairly constant level. When the supplies in the food are insufficient, the skeleton is called upon to keep the level of blood calcium within normal physiological limits, so that whenever the body goes into "negative balance," either for calcium or for phosphorus, the skeleton begins to suffer. When absorption of minerals from the intestine does not balance elimination in milk and excreta, the physiological demands are met by mobilisation of skeletal reserves. The osseous tissue is broken down to liberate the requred elements, and defects or cavities are left in the texture of the tela ossea. This process is known as " resorption," and is quite normal within certain fairly wide physiological limits. The converse is " deposition," in which osseous tissue is laid down and immediately impregnated with minerals to give a denser bone. Under normal conditions resorption and deposition succeed one another: they are of every-day occurrence, and balance out over short periods of time as long as the animal lives, although the capability of rapid response tends to diminish with advancing age. It must be emphasised that the process of mobilising is not one of "leaching out" of osseous tissue, leaving ossein behind. It is quite definitely a destructive one, and every time minerals are withdrawn an actual breakdown of bone occurs. A leaching-out process, known under the term " halisteresis," was at one time supposed to occur,

and thought to be responsible for the appearance of "osteoid tissue," but this is no longer accepted as a normal phenomenon. When osteoid tissue appears in a bone in abnormal amounts it is the result of a complete breakdown, followed by deposition of fresh material, which fails to calcify—a point to which I shall return when discussing rickets and osteomalacia.

So long as the two processes—resorption and deposition—occur more or less contemporaneously, or follow one another within a reasonable time interval, such as one lactation season, no gross changes will be observed in the general structure of the bones. But the moment a clear disproportion occurs, either through increased resorption or decreased deposition, definite changes will follow. In the long run the effect on the texture of the bone is the same in both cases, and the total amount of bone tissue becomes reduced. The result is a reduction in the weight and an increase in porosity of the bones, although it may often be difficult to say where the normal ends and where the abnormal begins. The changes can be best observed in comparing bones of animals fed on mineral-deficient rations with those of animals fed on rations adequate in minerals, preferably with a wide range between extreme deficiency and optimal nutrition. My experiments with Green and du Toit, to which I shall have to refer on several occasions in the lecture, provided skeletal material suitable for detailed histo-ogical study.

Two of the heifers in these experiments received about 37 g. CaO and 28 g. P_2O_5, mostly in the form of bone meal, and during the period of observation developed at a normal rate, became pregnant, and calved normally. One increased from 350 lb. in September, 1924, to 1,220 lb. in December, 1926; the other from 580 lb. to 1,180 lb. over the same period: both satisfactory for the class of animal concerned and the kind of ration fed. The heavier of the two was killed and the skeleton prepared for examination. Of all the animals it had the heaviest bones. The metacarpus and metatarsus had the thickest compacta and trabeculæ, the smallest medullary cavities and medullary spaces in the cancellated tissue. A polished section of the compacta had the appearance of ivory, and some portion of the epiphysis almost suggested a sclerotic condition. This bone probably represented the maximum possible production of osseous tissue and maximum storage of minerals. Since, as already pointed out, the architecture of bone is partly governed by functional influences of a mechanical nature, I paid special attention to the distribution of bony tissue in relation to reservoirs of calcium and phosphorus. The new tissue was laid on to the walls of the medullary cavity and the spaces of the spongiosa, increasing the thickness of the compacta and of the trabeculæ, and reducing the diameter of the cavities. It filled, so to say, the clefts between the trajectories. Deposition was most marked in those portions of the bone subjected to most pressure and torsion, such as the subarticular regions of the proximal ends of the metacarpus, metatarsus and phalanges. In these places the trabecular network was exceptionally dense, the medullary spaces being reduced and the structure resembling that of compacta.

As already mentioned, the process of deposition consists in laying down lamellæ through the activity of osteoblasts, which arrange themselves in regular rows, thus marking the lamellation. Wherever the deposition of lamellæ takes place upon a surface which has been previously resorbed, a definite line of demarcation or "cement line" is produced, separating the new from the old bone. In places where osseous deposition is actually proceeding, a narrow seam of osteoid may be observed. This is newly-formed bone substance, and the presence of occasional thin layers of osteoid tissue is a normal feature of a growing bone. The deposition of lamellæ is most conspicuous in the medullary cavity of the diaphysis, giving the surface of the bone a smooth appearance, and these "internal lamellæ" represent a considerable portion of the total stored mineral reserves.

According to this description it is possible to judge the amount of reserves in the bones from the thickness of the osseous layers and the diameter of the cavities. In our well-fed control, just referred to, microscopical examination of a typical bone showed the spaces well rounded, smooth and generally small. There was some evidence of resorption and reconstruction, both in the trabeculæ and in the cortex, which could be interpreted as signs of response to mechanical stimuli; changes to which the architecture of bone is continually subject, but which are most marked during the period of development. Resorption in the compacta of the diaphysis is most often observed in the centripetal regions of the periosteal systems, where spaces are excavated and subsequently filled in with lamellar substance, finally forming Haversian tubes. Resorption can also be observed in portions of the cortex to which ligaments and sinews are attached and which undergo fortification by replacement of periosteal systems with Haversian systems. All these processes of resorption are normal, and occur in well-nourished animals as well as in animals receiving less than the normal amount of minerals. Whenever the mineral supply is definitely below physiological requirements, however, the resorptive processes are much intensified, and it is often possible to read the recent nutritional history of an animal in the histology of its skeleton. In this connection two heifers on low-calcium intake in the experiments under discussion are of interest. Both received only 8.2 g. CaO per day in their food, a quantity far below what they would get in any naturally occurring calcium-poor pasture. Of phosphorus they received 24g. P_2O_5, a quantity greatly in excess of the calcium and sufficient for slow growth and maintenance. At the beginning of the experiment one was fourteen months old and the other twenty months. Both heifers did surprisingly well: one increased from 470 lb. to 1,240 lb., and the other from 480 lb. to 1,320 lb. in twenty-two months. Both became pregnant, and one calved normally, but the other, the heavier of the two, had difficulties with the afterbirth after delivering a normal calf, and contracted a septic metritis, to which she succumbed after twenty-eight days' illness. The skeleton of the animal was prepared for microscopical examination. The macerated bones were somewhat lighter than in the control animal mentioned above, which received over four times as much CaO, but the marked differences in relative measurements were much more significant than the difference in weight of the

skeleton. The diameters of the corticalis of the metacarpus and metatarsus were considerably reduced; the width of the medullary cavity was correspondingly increased and extended into the epiphysis. The medullary spaces of the cancellated tissue were larger, those in the central portion of the epiphysis were more or less coalescent, and those of the marginal portion encroached on the corticalis. The surface of the medullary wall was roughened, and showed small grooves separated by low ridges. The roughness of the inner surface of the diaphysis in the macerated bone was in marked contrast to the corresponding surface in the control animal and clearly indicated resorption. Microscopical findings confirmed the macroscopic appearance. The internal lamellæ of the diaphysis in the metacarpus and metatarsus had been removed, leaving an irregular resorption line cutting through the zone of the Haversian systems. Resorption was also marked in the subchondral regions of the joints, which were invaded by the enlarged medullary spaces of the epiphysis. Haversian spaces appeared in increased numbers in the inner portions of the diaphysis of some of the long bones, such as the humerus. The trabeculæ of the spongiosa of all bones showed thinning, erosion, and frequent perforation by capillaries. In the flat bones, such as the scapula, ribs, pelvis and olecranon, the trabecular reticulum was discontinued. In contrast to these evidences of breakdown, signs of deposition were rare, and very few layers of osteoblasts could be observed. The animal on the calcium-deficient ration thus showed a marked discrepancy between the two opposing processes of resorption and deposition which in the normal animal are well balanced. In pathology such a discrepancy, in which resorption exceeds deposition, is termed atrophy, and is a stage in the development of a retrogressive process, which in a more advanced stage is termed osteoporosis. Unfortunately the case was complicated by a metastatic septic metritis, which led to hyperæmia and exudation into the marrow of the cancellated tissues, especially of the ribs and vertebræ, so that the interpretation of the atrophy was somewhat obscured. But although the general phlegmasia was doubtless partly responsible for the removal of tela ossea, it was of short duration, and can only have operated to a very limited extent. This conclusion is supported by a parallel case of metastatic sepsis of equal duration and of fatal issue in a case of the same age in the early stages of aphosphorosis. Here the atrophy was less marked, although from the incipient clinical symptoms of phosphorus deficiency it might have been expected to be greater, so that the metritis of the low-calcium cow probably did not contribute much to the existing bone atrophy.

The experiments in our series also included animals fed on rations containing sufficient calcium but insufficient phosphorus, and animals fed on intermediate quantities of both elements. The detailed results come in for later discussion, but at this point it may be stated that whenever phosphorus was deficient, rickets and osteomalacia developed. In the early stages of our experimental aphosphorosis clinical symptoms of pica or, more specifically, "osteophagia" appeared, an occurrence we anticipated from our experience of the prevalence of osteophagia in cattle grazing over phosphorus-deficient pastures in South

Africa. The histology of the bones of two such animals is of special interest. One had shown osteophagia for a considerable length of time, the other had only recently commenced bone chewing. The calcium supply in the ration was adequate, so that the lesions can be attributed to deficiency of phosphorus alone. In both cases the changes in the bones were fundamentally the same as those in the calcium-deficient cow, although much more pronounced in the animal which had shown osteophagia for the greater length of time, and in which the lesions approached the stage of osteomalacia. In the less affected animal they were not prominent, and really only noticeable when compared with bones of the control animal. Macroscopically the lesions were discernible as a reduction in the diameters of the compacta and trabeculæ, and a roughening of the surface of the medullary cavity. Microscopically the lamellar lining showed distinct erosions most pronounced in the medullary cavity, in which it was almost completely eaten away. In the more advanced case, osteoporotic lesions were conspicuous, the bones were lighter, the compacta and trabeculæ were thin, and the medullary spaces were enlarged, but resorption had not yet reached the maximum possible for an animal suffering from extreme mineral deficiency. Later I will describe cases in which osteoporosis was still more advanced, and in which osteomalacic lesions, with abundant uncalcified osteoid tissue, finally superseded the reduction of osseous tissue.

From these examples it is evident that deficiency of calcium in the ration, and particularly deficiency of phosphorus, leads to atrophy of the skeleton. If sufficiently advanced this atrophy is termed osteoporosis, and a definite sequence of events may be traced. The resorptive process begins in the walls of the cavities, and proceeds centrifugally. It is most pronounced in the compacta of the diaphysis, where the inner lamellæ are first removed. Haversian spaces then appear within the adjacent zone, extend into the outer zone of periosteal systems and remove the osseous tissue, leaving cavities. These cavities are, in my opinion, identical in nature with the so-called " perforating canals " which penetrate the trabeculæ of the cancellated tissue, which they enlarge and break into fragments.

The experimental data at my disposal also indicated that increased resorption is most pronounced on a mineral-deficient ration when the drain of lactation imposes the greatest physiological demand for calcium and phosphorus. Even the normal cow, which, as already mentioned, may pass into negative mineral balance at the height of lactation on ordinary rations fairly rich in calcium and phosphorus, probably shows a considerable degree of osteoporosis. The modern dairy cow, bred for high milk yield, is an animal in which the capacity for expending minerals *via* the udder may exceed its capacity for absorbing minerals from the gut. The skeletal reserves will then be called upon at every lactation, and the bones suffer atrophy in proportion to the difference between minerals secreted in the milk and the minerals absorbed from the food. During the dry period there is an opportunity for deposition to replace the losses from resorption, so that the texture of the skeleton swings between a normal state before each lacta-

tion and an osteoporotic state at the height of milk secretion. Variations of this magnitude cannot be called pathological unless we are prepared to admit that the modern dairy cow is a pathological animal, and we must therefore allow considerable variations in bone texture to be classed as " within the physiological limits." But when reserves really approach exhaustion point the atrophy becomes so pronounced that there can be no mistaking it as anything but pathological. Osteoporosis may develop in an alarming manner, producing a fragility of bone which leads to actual fractures. In the German-speaking countries the condition goes under the descriptive name of " Knochenbrüchigkeit " (brittle bone), and in South Africa it passes under the name " stijfsiekte " (stiff sickness). Nature attempts to prevent the danger by laying down new tissue, the calcification of which, in absence of sufficient minerals, is defective. An attempt is made to rectify the excessive absorption by deposition, but since the mineral units for proper construction of osseous tissue are missing, an excessive quantity of osteoid is laid down. I shall return to this when discussing osteomalacia in more detail.

Within my own experience atrophy of the skeleton of ruminants, particularly of cattle, has always been the result of mineral malnutrition, but other causes of atrophy have been described in man and in animals. A " marantic atrophy " has been described found in general starvation, and supposed to be due to lack of nitrogenous substances and reduced production of bone. Other atrophic conditions are found, particularly in old age, called senile atrophy, and apparently independent of dietary deficiency of minerals. This type has received a great deal of attention in human pathology, but very little in the veterinary province, where it is naturally rare and practically only found in old pets whose span of life is unduly prolonged. Senile atrophy is said to be characterised by thinness of the lamellar layers of bone tissue, which are separated by " cement lines," and is explained as a disproportion between deposition and resorption of osseous tissue, in which the latter proceeds normally, while the former does not. This is Pommer's original view, and is widely accepted. Atrophy is also said to occur as the result of inactivity, or lack of trophic stimuli, as in the case of bones of the extremities which for any reason have been immobilised. Such unused bones may become porotic and subject to fractures ; in them the atrophic state of the tela ossea would be the result of hypoplasia, and thus differ fundamentally from the atrophy I have described. Resorptive processes in the bone are called osteoclastic, and are either of cellular or vascular origin. Osteoclastic activity is generally associated with the presence of multinuclear cells called osteoclasts, but it would appear that the removal of bone tissue is not their exclusive monopoly, and that mononuclears can also take part. Pommer rightly points out that the function of a cell must be related to its apparent activity, so that when we find cells clearly fitting into a lacuna, we are entitled to conclude that they are osteoclastic. In vascular activity the cells of vessels, capillaries and lymph spaces can also be osteoclastic, and there is indeed a view which treats the two resorptive processes as philogenetically the same, and " osteoclasts " as nothing

more than detached sprouting vascular cells. The resulting cavities are generally called " Howship's lacunæ," and are most distinct and sharply circumscribed in cases of polynuclear osteoclastic activity. Vascular activity is less conspicuous, and where a vessel runs along a trabecula the grooves are not so noticeable, although the process is quite obvious whenever the capillaries actually enter the osseous tissue and perforate it, producing the so-called " Volkman canals." In the atrophic process due to mineral starvation, the osteoclasia by multinuclear cells is by no means conspicuous. I have not observed a great increase in their number, and Howship's lacunæ were not characteristic in any of my cases. There was more evidence of vascular resorption, and I concluded that the breakdown of bone tissue for the purpose of mobilising mineral reserves is fundamentally a vascular process. Multinuclear cells, however, were visible in the ossification zone of the epiphyseal lines, where cartilage-carrying osseous septa was being removed and replaced by lamellar trabeculæ.

Experimental research by various investigators has shown that hyperæmia of the bone tissue is succeeded by porosity, and the dilatation of the vessels has been explained as being of neuroparalytic origin. Vasodilatory influences are general concomitants of inflammatory conditions, and their effect is frequently observed in localised foci. That a generalised osteoporosis, due to phlegmasia affecting a whole skeleton, and thus revealing itself as a generalised disease of the whole system, does occur in cattle is shown by an accidental occurrence in our own series of experiments. In the article already referred to—" Minimum Mineral Requirements in Cattle "—one of the heifers on a ration deficient in both calcium and phosphorus developed symptoms of skeletal disorder at a much earlier date than her mate on the same ration. At the time this was thought to represent a typical case of " stijfsiekte," and was so recorded in the original paper. But, as will be shown later, the disease "stijfsiekte" is a true osteomalacia, and subsequent study of the disease of this animal showed a different picture. Although chronic in its evolution, the disease had a more rapid course than the true osteomalacia which developed later in its mate, and symptoms of stiffness and tumefaction of the joints were already marked in the thirteenth month of the experiment. On account of extreme cachexia the animal was killed in the seventeenth month. Its mate was reasonably healthy at that time, only showed clinical osteomalacic stiffness in the twentieth month, and was not destroyed until twenty-four months after deficient feeding was begun. As compared with its mate, and also with other animals which developed symptoms on rations of various degrees of mineral deficiency, the course of disease in this heifer was abnormal. The real nature of the case was not realised at the time, and only became clear when the bones were sectioned for microscopical examination. Of all the animals studied, it showed the most advanced osteoporosis. Röntgen photographs of the metacarpus and metatarsus showed unusual transparency and very thin compacta. Macerated bones showed separation of the epiphysis and diaphysis in the subchondral region of intermediary cartilage, resulting from an inflammatory process which led to necrosis of the endochondral trabeculæ

of the metaphysis and to proliferation of cartilage. The lesions were present in all epiphyseal cartilages in all parts of the skeleton, but were most pronounced in the red marrow, *e.g.*, in the vertebræ and the flat bones. The marrow was soaked in a serous fluid, which impregnated everything, and in some places the lymphoid tissue was replaced by serous lagoons. The fluid penetrated the vascular canals of both Haversian and periosteal systems and impregnated the periosteum. The serous lagoons contained long filaments of fibrinous coagula, and small foci of polynuclear leucocytes were apparent in the vertebræ. The bones were unusually light, the scapula was transparent in its thinnest parts and thickened towards the proximal margin ; the bones of the pelvis joined at an acute angle, forming a keel. The corticalis of some bones of the macerated skeleton, particularly the flat bones of the pelvis and scapula, peeled off in large pieces. Several ribs had been broken, and the cancellated tissue of the flat bones was so brittle that it could be rubbed into powder between the fingers. The lesions of an excentric atrophy were everywhere marked. In the diaphysis of the long bones the medullary lamellæ and a portion of the Haversian zone had disappeared. Haversian spaces penetrated into the outer zone almost to the periphery. In some of the bones the formation of new periosteal systems was apparently still taking place, but the process was incomplete, the vascular canals were wide open, and the picture somewhat resembled that seen in a neonatus. Atrophy of the tela ossea occurred throughout the entire skeleton, but was more pronounced in some bones than in others, the flat bones appearing to suffer most. The inflammatory process had extended to the surface of the bones, and a sequel to this was the appearance of osteophytes. They were responsible for thickening of the extremities, and were made up of flat layers, usually consisting of only a few superimposed periosteal systems with wide vascular canals, or a network of trabeculæ of fibrocellular origin with serous exudate in the meshes. The deposition of osteophytes was generally associated with the attachment of ligaments, but they were also found in other places where there was no evidence of traumatic influences. I consider them to be of inflammatory origin due to periostitis, and connected with the cause responsible for the extreme atrophy of the tela ossea and necrotic changes in the growing zones of the epiphyseal cartilages. In some places the osteophytes were simply superimposed on the intact surface of the compacta, but in other places the corticalis had first been removed, so that a continuity could be observed between the medullary spaces of the epiphysis and those of the osteophyte. With few exceptions practically all newly-formed osseous tissue was calcified, including the trabeculæ in the growing zone of the metaphysis, where endochondral bone formation had ceased as a sequel to the inflammatory process, and had been replaced by new bone of fibrocellular origin.

I have described the case of this animal in detail for three reasons : firstly, because it seems to be unique—I have been unable to find anything like it in the veterinary literature ; secondly, because it is important from a differential diagnostic point of view—it showed lesions which could be mistaken for those of rickets and osteomalacia ; thirdly, because it constitutes a very good example

of a far-reaching osteoporotic condition of inflammatory origin, representing a phase in the evolution of an osteodystrophic disease, the ætiology and true nature of which are not clearly known. The lesions in the growing zones of the intermediary cartilage resembled somewhat the inflammatory changes in cattle succumbing to septic metritis, since here also metastases are formed in the epiphyseal lines, and in the myelogenous tissue of the vertebræ and ribs, forming serous lagoons and fibrinous deposits accompanied by hyperæmia and hæmorrhage. The analogy is strong, and it is tempting to treat both processes as identical, especially as there was some evidence in the anamnesis to support the similarity in the histological appearance. Five months after entry into the experiment the animal showed symptoms of metritic disturbances which recurred at intervals and finally disappeared without discovery of the cause. Since the intermediary cartilages of the metapodium, which normally ossify at the age of about twenty-four months, were affected, but not those which ossify at an earlier period, it was clear that the process began when the animal was about two years old. The first clinical symptoms were noticed in the fifth month of the experiment, when the animal was about twenty-five months old. It is therefore evident that the infection was either already present on entry into the experiment, or occurred not long after. The metritic disturbances cleared up and the animal recovered, but it subsequently failed to conceive despite two services. The assumption that we are dealing with a generalised metritic metastasis is therefore the most likely explanation, although it is not the only one which can be put forward.

Generalised osteodystrophic diseases occurring after metritis have not been described elsewhere in the veterinary literature, although metastatic conditions in joints and other organs are not rare sequelæ. From the point of view of differential diagnosis, the possibility of interpreting the observed process as a form of osteodystrophia fibrosa should also be considered, although it differs from the picture of that disease by the presence of the marked inflammatory and necrotic lesions.

With regard to other animals, osteoporotic conditions have been observed in experimental studies in dogs and the usual small laboratory animals as a result of dietary deficiency of minerals. The studies were mainly undertaken to throw light on the ætiology of rickets. Some of them were carried out before the significance of the vitamin factor was understood, while others were undertaken for the express purpose of determining the influence of this factor. When mineral deficiency was under consideration, stress was usually laid upon calcium, and in the older literature insufficient attention was paid to phosphorus and the mutual relationship between calcium and phosphorus. In most cases of mineral deficiency osteoporotic conditions were observed, and were sometimes referred to " pseudo-rachitic osteoporosis " to indicate that there were also changes in the intermediary cartilages. But they were not considered to be genuinely rachitic, because the pathognomonic osteoid formation was absent, or the amount of osteoid was not considered sufficient to justify a diagnosis of rickets. Besides the lesions of

osteoporosis, some cases showed alterations of the marrow, fibrous tissue, and increased multinuclear osteoclasts, so that the picture would resemble osteodystrophia fibrosa. The early experimentators did not make this diagnosis but Christeller, in reviewing the literature, called attention to the prevalence of, osteofibrotic changes. Pictures resembling Barlow's disease in children are also recorded in the earlier experimental animals. In all the conditions described, osteoporosis was apparently the most striking lesion, but never seems to have been the only change. Osteoporotic lesions were also produced in rats fed upon synthetic rations, where it would appear that calcium deficiency was generally the responsible cause. In the case of experimental scurvy in guinea-pigs, produced by rations deficient in vitamin C, osteoporotic lesions were also found. Similar lesions are recorded for pigs, and attributed to scurvy, although we now know that avitaminosis C does not occur in pigs. Since vitamin D plays a rôle in the fixation of minerals, and its absence leads to rickets and osteomalacia in the human subject, vitamin D deficiency would also be conducive to osteoporosis. Although osteoporosis is always found in osteomalacia of man, it is not considered by human pathologists to be a characteristic change in human rickets. In the experimental rickets of the dog it occurs, but is not a constant lesion. It is, however, a very marked feature of the osteodystrophia fibrosa of equines, goats, pigs and dogs, a disease now classified apart from true osteomalacia. It is also a marked feature of "stiffsickness" of cattle, a condition of widespread occurrence on deficient pastures in various parts of the world, but is then only a stage in a syndrome called aphosphorosis, which ends with osteomalacia in adult animals, or rickets in young animals.

In reviewing the facts I have brought forward about osteoporosis, I may summarise by pointing out that only in rare cases does it appear as a final and uncomplicated pathological state, *e.g.*, in the hypoplasia of senile and marantic atrophy, where it is the result of decreased synthesis associated with normal resorption. In all other cases it appears to be the result of increased resorption, be it physiological, as in the case of increased mobilisation of minerals to meet the drain of lactation, or during temporary dietary mineral deficit due to seasonal changes in composition of pasture; or be it pathological, as in the case of inflammatory conditions of the medullary tissue, leading to hyperæmia and increased vascular activity. Osteoporosis therefore appears to be in most cases a transient stage in the evolution of some disease the last phases of which are not always reached and hence not always definitely recognised.

(2) Rickets and Osteomalacia.

In human medicine the terms rickets and osteomalacia are used to designate a specific condition affecting the whole skeleton: the former name being used for the disease as it occurs in children, and the latter for the form found in adults. The similarity in the pathological picture of the two differently named diseases was recognised at an early date, and the pathologists were impressed by the presence of a superabundance of uncalcified osseous tissue (osteoid) in both cases. The difference was thought to be in the genesis of the osteoid tissue, and Virchow explained it as a result of non-calcification of newly-formed osseous tissue in infants, but as a result of decalcification of fully-formed bone in adults.

It was subsequently realised, however, particularly through the researches of Pommer, that in the normal growth of bone breakdowns and rebuilding of the tela ossea take place alternately at varying rate all through life, and that the deposition of uncalcified tissue in small amounts is a transitional stage in the process of growth. Views on the genesis of osteoid therefore changed, and the presence of excessive quantities is now considered to be the result of non-calcification of new tissue, and not of decalcification of previously existing bone. A process of decalcification, known under the name of "halisteresis," is still considered to occur by one school of pathologists, but the view is strongly contested by another school, which has the weight of evidence in its favour. Lack of calcification, however, is not limited to newly-formed osseous tissue, but is also observed in the region of the proliferating intermediary cartilage, known as the "provisional zone of calcification," and it is here that the series of changes occur which are typical for rickets. So long as the provisional zone is present and growth of cartilage is taking place rickety changes can occur. In man this period lasts up to the age of twenty, and sometimes even beyond that, although the rate of growth of cartilage diminishes rapidly with age. Human pathology distinguishes "rachitis infantilis," or rickets occurring in infants between the age of four months and two years, from "rachitis tarda" or rickets of adolescents.

As the cartilaginous centres of growth ossify with advancing age, the chances of becoming affected diminish, and hence the changes characteristic of rickets are no longer observed, while those resulting from non-calcification of the tela ossea dominate the pathological picture. The disease is then called osteomalacia.

There is therefore no fundamental difference in the pathological state of the skeleton in the two differently-named diseases, and a definition which takes a superabundance of osteoid tissue, transcending all normal physiological limits, as the characteristic lesion, irrespective of age, has the advantage of describing the actual state of affairs without prejudice to subsequent explanations of causation. In veterinary medicine the two terms have also been used to describe a pathological condition in young and in adult animals. Rickets is referred to as a disease of foals, calves, lambs, kids, young pigs and puppies, and osteomalacia as a disease of horses, cows, sheep and goats; less often of pigs and dogs.

As a criterion of adult age, sexual maturity is often taken without due consideration of the state of the skeleton at the time. But sexually mature animals may still be growing, and a cow, for instance, may have had two or even more calvings before all the intermediary cartilages have ceased proliferation. If during this period these centres of growth are subjected to conditions which cause defective calcification, the animals would, strictly speaking, be suffering from rickets. This is quite often the case, but the apparent misnomer " osteomalacia " for the disease in adolescent bovines has no practical consequences, since the fundamental conception is correct from the pathological point of view, and, as we shall see presently, also from the ætiological standpoint. In veterinary medicine we are therefore justified in continuing to use the customary clinical names.

In their book " Die Rachitis," Marek and Wellmann emphasise the fact that the rate of growth of our young domesticated animals is considerably greater than that of children. Growth is about four times as fast in the horse, four and a-half times in cattle, six and a-half times in sheep and goats, ten times in pigs, and thirteen and a-half times in dogs. Hence these animals have a more advanced skeleton by the time they are usually exposed to conditions which give rise to rickets, and the disease therefore evolves in a more mature bone. The resulting lesions should therefore be comparable with those of " rachitis tarda " in man, and this is actually the case in animals whose growth rate is slowing down. But in my opinion it is not the case in so far as dogs and pigs are concerned, since puppies and piglets are generally exposed to factors causing rickets while the proliferation of cartilages is still proceeding actively. The lesions then show all the characteristics of florid rachitis.

The ossification of the various cartilages occurs according to their topographic position at more or less definite periods in different species, and even in different breeds of animals. The cartilages in the proximal bones of the extremities close at the age of about eighteen months in the dog, but only after three to four years in the herbivora. The ossification of the tubera of the pelvis takes place later, at about the time when the cartilages of the vertebræ close, *i.e.*, in the dog at about twenty to twenty-four months, and in equines, ruminants and pigs at the age of four to six years. In the ribs the sternocostal cartilages still show proliferations after the growth of the extremities has ceased, and hence typical rachitic lesions may be found there even at an advanced age.

It is only to be expected that considerable variations in the pathological picture of rickets will be found in different animals, not only as a result of differences in their intensity of growth, but also as a result of external influences and mechanical factors. The larger domesticated animals are on their feet from birth, and are generally very active at the age when they are exposed to the conditions inducing rickets. The cartilages are therefore exposed to injuries comparatively early. Animals which reach sexual maturity at an early age, and which are used for breeding long before their growth has ceased, are exposed to the strain of pregnancy

and lactation while the cartilaginous centres are still proliferating. Milk production tends to divert minerals from the proliferating centres, and when the food supply is on the borderline of mineral deficiency, lactation may be the precipitating cause of rickets.

Attention should also be drawn to some histological features peculiar to certain species of animals, in which bone resorption by osteoclastic activity is normally increased during the earlier periods of life. Marek and Wellmann have pointed this out for pigs and dogs, and attach considerable importance to this phenomenon. In these animals osteoclastic activity begins within the first few weeks after birth, and continues for several months, thus falling within the period of development of rickets. The process is characterised by the presence of numerous multinuclear osteoclasts, the actual number varying in different portions of the same bone. The osteoclastic activity is greatest in the metaphyses of the long bones and homologous portions of the ribs, places where the primary bone deposits undergo resorption during the period of longitudinal growth and are replaced by the more permanent spongiosa. Osteoclasts may also be found in great numbers in other localities, such as the subarticular regions and the tissue of the dental alveoli.

An apparently increased osteoclastic activity in a rachitic bone of a young pig or puppy need, therefore, not necessarily indicate a pathological resorption, but might itself be a normal phenomenon. I have observed a similar augmented osteoclasia in the diaphyses of the bones of a calf fœtus and in the subchrondral zone of the bones of older bovines, both normal and rachitic, but could not find increased numbers of osteoclasts in other parts of the same bones. I attach considerable importance to this observation, since it is in conformity with the general findings in human rickets, in which paucity of osteoclasts is generally commented upon as a feature distinguishing the disease from other osteodystrophic disturbances.

Animals are generally subject to rickets only after weaning, but the question is often raised whether the disease is hereditary or, more accurately, whether animals can be born with it. Indeed, there exists the term " rachitis congenita," but the pathological picture of that disease does not correspond to true rickets, and should be described as " chondrodystrophia fœtalis hypoplastica," a name which indicates a defective development of cartilage. In so far as bovines are concerned, I can state on the basis of carefully controlled laboratory experiments by my colleagues and myself at Onderstepoort, and careful observation in the veld, that no calves are born with true rickets. Any superficial suggestion of rickets could be negatived by closer study, and the whole South African experience shows that a cow suffering from extreme osteomalacia will throw a normal calf so long as she can give birth at all. A series of comparative observations on calves born from osteomalacic and from healthy cows showed the same average weight at birth and the same blood picture in respect of mineral constituents. Apparently the mother sacrifices herself for the fœtus.

With regard to equines, I do not think that true osteomalacia has yet been recorded, although the name has been, and still is, applied to an abnormal condition of the skeleton, characterised by deformation of the head and porosity of the skull. This disease is known in France under the name of "cachexie osseuse," and by various other names in different parts of the world. It has been described by several observers (including myself, in South Africa) as osteoporosis, most of whom realised that the changes did not correspond with those of osteomalacia in other animals, and concluded that it was an ætiologically distinct disease. It is now classified under the heading of "osteodystrophia fibrosa," and I shall describe it in detail when dealing with the group of diseases to which it really belongs. But the misleading term "equine osteomalacia" should be abandoned, since in the whole veterinary literature there is no satisfactory evidence that such a disease has been described. Its existence has not yet been demonstrated by histological examination, the only test which allows us to use the term osteomalacia according to its strict pathological definition.

Joest and Zumpe drew attention to this fact long ago, and even went so far as to doubt whether rickets and osteomalacia, as used in the medical sense, really existed in the domesticated animals at all. But, as I shall show later, their doubt is certainly unfounded, and the "stijfsiekte" of bovines in South Africa fits the classical pathological description in the human subject.

It has frequently been stated that osteomalacia occurred in grazing cattle, while absent in horses running under the same conditions, and, conversely, that osteomalacia occurred in horses, while absent in cattle exposed to the same environment. So long as osteoporosis in horses was considered to be the same as osteomalacia in other animals, and to have the same cause, the absence of one disease and the presence of the other must have been a puzzling problem; but now that we know them to be pathologically and ætiologically distinct, the apparent discrepancy disappears.

In relation to these two diseases the experience of South Africa is of interest. At one time both occurred simultaneously within the country, but while osteoporosis of horses has entirely disappeared, osteomalacia in cattle is still prevalent. The equine disease appeared sporadically in stables, but never amongst grazing horses; while the bovine disease occurred in pastured cattle, and was associated with certain types of veld. The two diseases were thus observed under quite different conditions, and it was shown later that bovine osteomalacia in South Africa is caused by deficiency of phosphorus in the pasture. This deficiency apparently does not affect equines to the same degree, and no osteomalacia is observed. Nevertheless, horses bred under South African veld conditions are frequently undersized and under-developed, and although there are no symptoms permitting a definite diagnosis, it seems at least possible that the stunted growth of horses is due to the same cause as the clinically apparent osteomalacia of cattle. Similar observations have been made in Australia, where it was found impossible to breed race horses in certain regions.

Rachitis and osteomalacia in bovines are widely recorded in the veterinary literature, and occur in all parts of the world, but the histological proof that their pathology conforms strictly to the definition of the corresponding diseases in the human subject has only recently been brought forward.

Rickets is often found in calves on phosphorus-deficient pastures. Under the ranching conditions of South Africa the calves are weaned at the age of about nine months, and by that time calves of osteomalacic mothers are certainly inferior in weight and size to calves weaned from mothers receiving a supplement of phosphate. The explanation, however, is not congenital inferiority, but simply that their growth requirements are not covered by the quantity of milk obtained from the mothers subsisting on the phosphorus-deficient pasture, and that they themselves have to make up too large a proportion of their food at too early an age from the same deficient veld. We noticed rickets particularly in calves which had lost their dams early in life and which received an inadequate share of milk from foster mothers. The same observation was made with calves whose mothers, for one or other reason, had bad udders.

Clinically, the disease in calves differed very little from that in young cows, although tumefaction of certain joints was perhaps more marked and persisted after recovery from rickets. Microscopically the changes found in heifers and young cows conform in principle to the definition of rickets in children, but there are certain peculiarities which appear to be typical for cattle and to which attention will be drawn later.

The position in ovines is similar to that in bovines. The disease has been described in lambs and ewes, and occurs in enzootic form in South Africa under similar conditions to those producing it in cattle. Marek and Wellmann have described the pathological picture of rickets in lambs.

The position in goats, however, is different. There is evidence to show that what has hitherto been described as rickets in goats is an affection often complicated with osteodystrophia fibrosa, and the pathological description given by Marek and Wellmann, as well as by Christeller, indicates that the disease is similar to that mentioned above for equines.

In pigs, rickets is well known; but here again the problem has only been cleared up in recent years by the separation of true rickets from osteodystrophia fibrosa, a disease which in the pig goes under the name of "Schnüffelkrankheit," or snuffles," although the same name is also used for a disease which is not an affection of the bones at all.

Rickets in pigs has been the subject of extensive researches by Marek and Wellmann, and their experiments are important from many points of view, but what interests us at this stage is the fact that the microscopical lesions observed are in complete agreement with the accepted histological definition of the disease. In addition there are certain other changes resembling those peculiar to cattle, and probably of similar origin. Of particular importance is the fact that in the course of their experiments cases were produced in which rickets

was complicated with osteodystrophia fibrosa. Of forty-one young pigs, seven showed this complication in more or less severe form, and occurred in diets differing very little from those which caused pure rachitic lesions.

Rickets in dogs is familiar to most veterinarians, and is perhaps the best known osteodystrophic disease of domesticated animals. Before the white rat came into general use the dog served as the experimental animal for the study of rickets, and a considerable amount of evidence is therefore available. Although the clinical picture of rickets in dogs appeared to permit of only one interpretation, the nature of the underlying pathological process caused much controversy. That true rickets, complying with the accepted histogenetic definition, did occur in dogs is shown by the evidence of medical pathologists, but many cases were called in question. For instance, the disease observed in the well-known experiments of Mellanby were regarded by Christeller as belonging to the group of osteodystrophia fibrosa. I, personally, have no doubt that Mellanby's dogs suffered from true rickets, and I base my opinion on the evidence of his pictures, which show increased osteoid tissue as well as other typical lesions. But Mellanby based his diagnosis mainly on the radiographic appearance, and on the low calcium content of the bones, which, as we now know, is similar in osteodystrophia fibrosa. He seems not to have been quite sure what the pathological picture in the dog ought to be, and although accepting Pommer's criterion of diagnosis from the presence of superabundant osteoid, he seems to have been uncertain in the interpretation of cases complicated by osteoporosis, a feature which leading pathologists of the time, such as Pommer and Schmorl, did not consider to be characteristic of rickets, but to be atypical.

In the earlier experiments of deficiency diseases artificially produced in dogs, some cases occurred in which osteoporosis alone was a conspicuous feature, while in others excess of osteoid tissue occurred as well. On account of the marked osteoporosis the disease was called " pseudo-rickets," and the presence of the osteoid tissue was explained as an incidental occurrence, due to the rapid development of the bones of the fast-growing dog. Indeed, the presence of osteoporosis in experimental animals fed upon mineral-deficient diets was considered to be evidence against rickets, in spite of the fact that in the literature on human rickets osteoporosis was often quoted, and a porotic form of the disease even distinguished.

Marek and Wellmann also seem to dissociate osteoporosis as a lesion of rickets, although they describe an osteoporotic form in dogs. Korenchevsky has scrutinised the literature on this aspect, and assembled a considerable series of rachitic cases showing osteoporosis; he points out that Schmorl himself described cases of most pronounced bone resorption in human rachitis tarda. If we consider that in osteomalacia of the human subject osteoporosis is one of the outstanding lesions and that rickets is fundamentally the same as osteomalacia, I fail to see why osteoporosis should ever be regarded as an abnormality in juvenile rickets. Its presence or absence is probably

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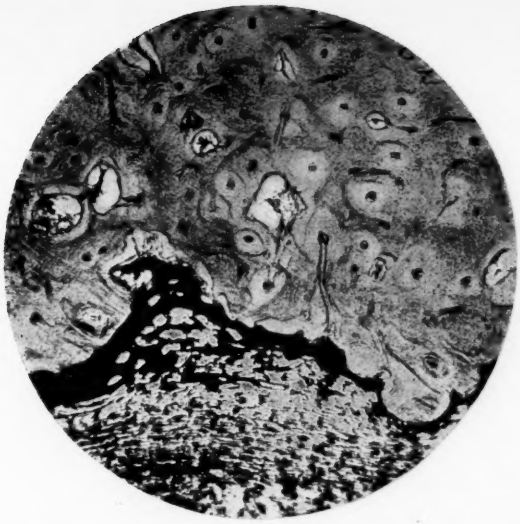

FIG. 9.—Heifer 759. Food deficient in CaO and P_2O_5. Metatarsus. Cross section. The lamellated medullary zone is eroded, and the medullary cavity encroaches on the zone of the Haversian systems. (Marked excentric atrophy.) The compacta shows various pores, some of which are lined with osteoid. (Osteomalacia.) Mag. 39 ×.

FIG. 10.—Heifer 1,020. Food with increased, but still insufficient amounts, of CaO and P_2O_5. Cartilage of the olecranon. Irregular process of ossification. The provisional zone of calcification is lacking, and the medullary canals enter in an abnormal manner into the cartilage. The subcartilaginous or spongoid zone consists of osteoid. Fibrillar marrow is present in the medullary canals. (Rachitis.) Mag. 63 ×.

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FIG. 11.—Heifer 759 (*vide supra*). Third rib, distal. A large medullary canal filled with endostal tissue, osteoblasts enter into the cartilage. The subchondral or spongoid zone consists of osteoid, which includes calcified portions of the cartilage. (Rachitis.) Mag. 63 ×.

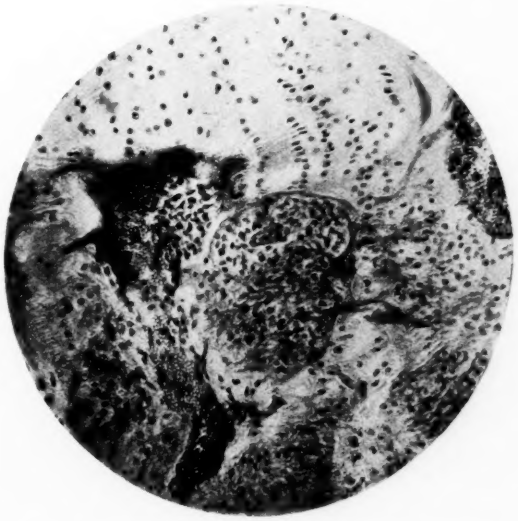

FIG. 12.—Heifer 1,020 (*vide supra*). Third rib, distal. A tongue of osteoblasts, including an osteoclast, enters into the cartilage. The black masses represent fibrillar endostal tissue. The vessel of a medullary canal is opened. (Rachitis.) Mag. 152 ×.

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FIG. 13.—Heifer 866. Food sufficient in CaO, but deficient in P_2O_5. Metatarsus, distal epiphysis. The subarticular zone shows numerous pores, of which those nearest the articular cartilage include fibrillar tissue. (Advanced porosis.) Mag. 39 ×.

FIG. 14.—Heifer 866 (*vide supra*). Third rib, proximal, in the vicinity of the tuberculum costæ. Marked atrophy of the spongiosa and deposition of osteoid tissue. (Osteomalacia.) Mag. 39 ×.

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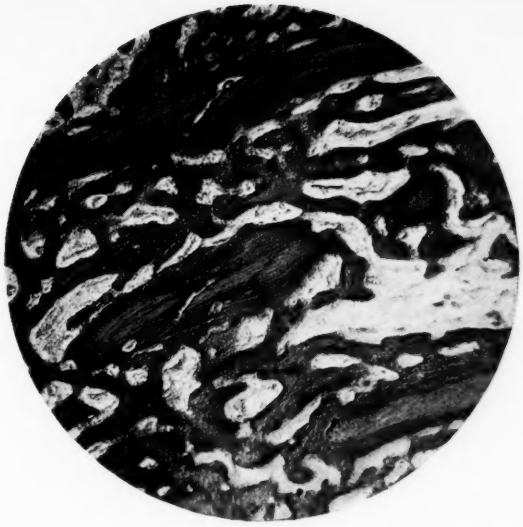

FIG. 15.—Heifer 866 (*vide supra*). Radius, distal epiphysis. Longitudinal section. Marked atrophy of the spongiosa; two trabeculæ show fissures. The space between the trabeculæ is occupied by an internal callus consisting of osteoid trabeculæ. (Osteomalacia.) Mag. 39×.

FIG. 16.—Heifer 866 (*vide supra*). Thirteenth rib, distal. Longitudinal section through the non-decalcified rib. The black parts are the only calcified portions of bone tissue. The section belongs to a callus, which consists entirely of osteoid. (Osteomalacic osteophyte.) Mag. 39×.

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FIG. 17.—Heifer 759 (*vide supra*). Tuber ischiadicum. Corticalis. The outer portion of the corticalis has been resorbed (concentric atrophy). The removed tela ossea is replaced by fibrous bone tissue, which lacks calcification. The osteoid includes a vascular canal, the course of which is apparently convoluted. A marked line of demarcation separates the osteoid from the calcified part. (Osteomalacia.) Mag. 63 ×.

FIG. 18.—Heifer 759 (*vide supra*). Tuber ischiadicum. Corticalis. Extensive formation of osteoid tissue in the fibrous bone and deposition of lamellated substance. The section shows a remarkably deficient calcification. Mag. 63 ×.

dependent upon the age of the animal and the degree of deficiency of the diet. According to my own experience, based upon experimental production of the disease in bovines by feeding on mineral-deficient rations, the osteoporotic condition is a stage in the development of rickets or osteomalacia in these animals.

For dogs the evidence of the literature not only points to the existence of true rickets, but also to the occurrence of osteodystrophia fibrosa, a disease which may be clinically mistaken for rickets.

Lesions.—The lesions of rickets and osteomalacia comprise disturbances in the intermediary cartilages, in the endosteum and the periosteum. They are all characterised by lack of calcification of newly-formed tissue. Defective deposition of calcium phosphate in the provisional zone of the epiphyseal cartilage is regarded as the beginning of all the disturbances occurring in these centres of growth, and as typical for the disease of rickets. This leads to an abnormal process of vascularisation, enlargement of the proliferating zone, and to production of osteoid tissue within and adjacent to the cartilage, giving rise to the so-called spongoid or rickety zone. If well marked, these changes can be recognised even by the naked eye in fresh bones. On the border of the metaphyseal spongiosa normal cartilage shows a fine white line, the calcification zone. This is absent or defective in rickets, and the cartilage itself is rendered more conspicuous by increased dimensions and frequently irregular borders. The subchondral zone shows a fleshy appearance and consists of soft tissue rich in blood and often hæmorrhagic.

Microscopical examination explains these macroscopic changes. In the proliferating and hypertrophic zones long cell columns are visible, frequently deviating in the shape of a fan as the result of bulging of the cartilage under pressure. The resulting epiphyseal thickening is most marked on the costo-cartilaginous joints of pigs and dogs, where it is called the "rickety rosary." The magnitude of the proliferation and enlargement of the cartilage varies in the different epiphyses, being well pronounced in those which close late, *e.g.*, the ribs and the tubera of the pelvis. It is less pronounced in the cartilages of the vertebræ, which seem more resistant to change. Since the bones of cattle have reached a more advanced stage of development than in the case of man by the time rickety changes appear, the thickening of epiphyseal cartilages in young bovines hardly ever reaches the magnitude seen in children.

Near its metaphyseal border the rickety cartilage is broken into tongues and islets surrounded by endostal tissue. This is caused by the proliferation of vessels which enter the cartilage in any direction in place of the regularly arranged primary canals of the normal bone. The calcified zone seems to be a barrier securing regularity of resorption, and in its absence the arteries and veins run anyhow, and can often be traced into the marrow of the metaphysis. In the cartilage they frequently take the shape of a tree with branches penetrating in all directions along and across the cellular columns. The tissue, which travels with the vessels and consists largely of endostal cells, proliferates and differentiates into osteoblasts,

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depositing osseous substance which does not calcify, and therefore remains osteoid. This tissue accumulates in the subchondral region and forms the "spongoid zone."

In the breaking-up of the cartilage pictures appear which could be interpreted as a metaplasia of cartilage into osteoid. Fine branches of advancing capillaries can be seen entering the cartilaginous cells and removing them. In the empty capsules osteoblasts appear and seem to undergo a change into osteocytes, whilst the hyaline ground substance seems to be transformed into osteoid. In sections stained with eosine the transformed cartilage takes the same red colour as the osteoid. The German pathologist, M. B. Schmidt, considers this metaplasia of the cartilage as the outstanding change in rickets, and traces the origin of the osteoid in the spongoid zone mainly to this process.

The description I have given of the pathological changes in the cartilages refers to cattle, but may be considered to apply to rickets of all domestic animals. The specimens examined, however, also showed certain other features, which have not been described in human rickets or in that of animals generally. My cases of rickets were produced by feeding heifers on a phosphorus-deficient ration over long periods—two years or more. The conspicuous difference in practically all the affected epiphyseal lines was the formation of a new cartilaginous tissue. This occurred in the abundantly proliferating endosteum, which enveloped the penetrating vessel and completely filled the cavities in the epiphyseal cartilage. The endosteum cells usually change into osteoblasts and produce osteoid, but in some of the cases under discussion they changed into chondroblasts, which crowded together, forming nests with very little ground substance between the cells. The resulting tissue was, therefore, a mixture of osteoid and cartilage, and pictures appeared adjacent to the old cartilage which were most difficult to interpret. In this process of new cartilage formation the connective tissue of the so-called cartilaginous canals also took part, and the phenomenon could be best observed in the sterno-costal and sterno-vertebral cartilages, where the cells occasionally arranged themselves into quite regular but small columns. In my opinion the formation of this pathological cartilage is the result of trauma, and is analogous to the behaviour in the callus of a broken rib where, on account of the instability of the fractured ends, cartilage is produced in place of normal tissue. I had occasion to observe the phenomenon in several broken ribs, in which the transformation of endosteum into cartilage, and of the latter into osteoid, could be followed in the same section.

Another conspicuous feature in my cases was the presence of much fibrillar tissue in the rachitic zone. In some places this formed a web enclosing endostal cells, and remnants of the web, apparently not used up in the production of endostal osteoid, were sometimes present in clefts formed by the filling up of medullary canals or spaces with osteoid or cartilage. The fibrillar structure thus marked off the boundaries between old and new tissue. The deformation of the rachitic zone and apparent compression of cells, cartilage and osteoid, with occasional blood extravasations, must be considered traumatic.

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In the bones of cattle the changes in the tela ossea begin with resorption, and lead to osteoporosis. I regard this simply as an exaggeration of the normal physiological process by which resorption of stored minerals occurs. Although the growth of the tela ossea is retarded under conditions of phosphorus deficiency, increase in volume does occur in course of time, but it is a remarkable fact that in none of our experimental cases was any significant deposition of osteoid observed on the inner surface of the walls of the diaphyses. Resorption was extensive, encroaching upon the Haversian region, which in some cases became so porous that a cross section presented a sieve-like appearance. Deposition of osteoid was conspicuous in the excavated Haversian spaces of the diaphyses, giving rise to osteoid Haversian tubes. Deposition of osteoid also occurred in the cancellated tissue of the epiphyses of the long bones, and particularly in the spongiosa of the flat and short bones. These parts of the skeleton represent the storehouse of the body for what may be called the more mobile portion of the mineral reserves, and they are therefore the first to show atrophy.

The newly-formed osteoid tissue was not uniformly distributed, some localities showing relatively excessive amounts which could frequently be associated with some injury. Remnants of fractured trabeculæ were found, and necrotic fragments were sometimes encased in the new tissue. Sometimes there were also signs of fresh or of old hæmorrhages. Such an accumulation of osteoid represents a hyperplastic condition within the bone, and in some instances can be classified as an internal callus. But accumulations were also found in places which showed no traces of previous damage, *e.g.*, in the spongiosa of the lumbar vertebra, the medullary spaces of which were sometimes completely blocked with new tissue.

As a rule, regular rows of osteoblasts deposit osteoid in uniform layers; but where massive production was observed it resulted from excessive proliferation of endostal cells, and did not present the appearance of lamellar deposition. The distribution of the cells was irregular, and the resulting tissue to some extent resembled a tissue of fibrous origin. The whole appearance suggested an emergency structure hurriedly laid down. The original medullary spaces were either completely blocked or reduced to mere clefts, and the structure sometimes even resembled that of the spongoid zone of the metaphysis. Although no calcification occurred in the greater portion of the new tissue, deposition of minerals did occur in some parts, usually following the axis of a trabecula. A remarkable feature was that in almost all places where excessive osteoid deposition had taken place active resorption was proceeding. From the larger medullary spaces and canals fine channels were driven into the osteoid, generally carrying a very thin capillary, ending blindly in the calcified axis of a trabecula. It was evident that the hasty emergency structure of massive osteoid, partially reinforced by localised calcification, was no longer needed, and was being removed. This resorption gave rise to all kinds of peculiar pictures, resembling lacework patterns and honeycombed nodules, the latter appearing to be the last residue of the emergency tissue. The process just described is also known in human rickets. It may occur in older children, and is called the hyperplastic form of rickets.

Periosteal changes appear with varying intensity. Just as the growth of cartilage in younger animals is not arrested, so also the growth of the bones in thickness goes on through the normal formation of periosteal systems. But calcification does not occur, or is imperfect, so that the new tissue remains soft. It is evident that injuries can then occur easily, and these lead to the formation of osteophytes, mainly in the epiphyses of the lower bones of the extremities around the joints. The thickenings so frequently found in cattle are caused by osteophytes, and in their simple form consist of superimposed periosteal systems localised in definite places, particularly at points of attachments of ligaments. The production of new periosteal systems is often irregular, and sections may present the appearance of trabecular lacework. The osteophytes are uncalcified, or only calcified in their deeper layers. An increase of periosteal osteoid tissue is particularly noticeable in the third phalanx and in the soles of animals, which showed pronounced stiffness during their illness.

In the experimental cases produced by Marek and Wellmann in dogs and pigs the rachitic lesions developed much faster, and the disease had a much more rapid course than in the case of the South African cattle. Their animals were also much younger and were exposed a much shorter time to injuries than were our calves, so that the lesions were less complicated by secondary traumatic influences. The rachitic picture was therefore simpler, and resembled that of human rickets more closely than that described by me for cattle.

We have seen that in cattle the pathological increase of osteoid affects the whole skeleton, but that under certain conditions it is more marked in some localities than in others, and that it is then associated with proliferation of the fibrocellular marrow. When the number of multinuclear cells is increased at the same time—an occurrence which may be normal in young animals—then the pathological picture somewhat resembles that of "osteodystrophia fibrosa," although, according to my experience, osteomalacia can always be distinguished from that disease by the quantity of osteoid tissue.

I have mentioned that enlargement of the proliferating zone of intermediary cartilage is one of the lesions of rickets. The enlargement in itself, however, cannot be taken as diagnostic, since it is found in other cases in which the process of endochondral ossification is interfered with. It is seen in Barlow's disease, in which the formation of osseous tissue is scanty, and in which the subchondral zones can suffer from traumatic injuries to such an extent that they become a mass of debris interfering with the growth of the bone. Production of osseous tissue is also hampered by any local inflammatory process, and I have had examples of this in some of my own cases, which were complicated with metritic metastases, and particularly in one case of generalised osteomyelitis. In this instance the zone of ossification was occupied by necrotic tissue, and the cartilage, the growth of which was not arrested, reached unusual dimensions. The calcification of the cartilage did not suffer, and deposition of minerals proceeded in successive provisional zones of calcification, as it does in cases of recovery from rickets.

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The clinical picture typical for rickets and osteomalacia can partly be deduced from the pathological changes. In cattle the artificially-produced disease and the one contracted spontaneously in the veld show the same symptoms, although the natural disease may be complicated by inanition. The absence of ossification in the intermediary cartilages and non-calcification of the osteoid leads to delay in development, to bending of the extremities, and to sinking in of the ribs with formation of the rachitic groove so often seen in the dog. Traumatic influences lead to a thickening of the epiphyses, caused either by the bulging of the softened cartilages, as in the case of the dog or pig, or by the appearance of osteophytic exostoses as in cattle. The soft osteoid tissue exposes the nerves to the influence of pressure, and stiffness and lameness follow. In order to relieve pain, animals take up unphysiological positions, which in their turn lead to malformation. Thus the claws of cattle and sheep are no longer worked off at the toes, and therefore grow long and deviate from the normal position. Pain in the feet forces the animals to stand still or lie down, or even to walk on their knees. Under such conditions feeding habits are interfered with, nutrition suffers, and the animals gradually become cachectic. Advanced atrophic and porotic changes cause fragility of the skeleton, and fractures may occur. In addition to these general symptoms there are others which vary according to the species of animal and are connected with the underlying metabolic disturbance and cause of the disease, *e.g.*, depraved appetite, or pica, in the case of cattle, to which I shall refer presently.

As already mentioned, the dog played the important rôle as experimental animal in the earlier researches into the ætiology of rickets; but it was subsequently found that the white rat was an even more suitable animal, and the lesions produced in it were considered to be identical with those in children. The results of Mellanby on the production of experimental rickets in puppies pointed to the absence of a specific food factor as cause of the disease, a " vitamin," the properties and distribution of which at that time appeared to correspond fairly closely with those recognised for vitamin A, but which is now known as vitamin D. Working on rats, Korenchevsky confirmed Mellanby's findings that, on a diet adequate in other respects, deprivation of a fat-soluble vitamin could be solely responsible for the production of rickets, provided the rats were not older than three to six weeks when the special feeding began. Subsequently a ration deficient in calcium, but otherwise complete, produced mild rickets and osteoporosis in some cases in rats, while a combined deficiency of calcium and vitamin produced rickets more effectively than either deficiency alone. In the experiments of Sherman and Pappenheimer rickets was produced in rats by a deficient diet, and then cured by the addition of potassium phosphate, so suggesting that phosphorus deficiency was even more important than vitamin deficiency. The extensive work of McCollum and other American investigators suggested that the relative proportions of calcium and phosphorus in the diet were of greater importance than their absolute amounts. In the absence of an adequate supply of vitamin D, the production of rickets could be accentuated by either an abnor-

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mally high or abnormally low ratio of calcium to phosphorus. Mellanby's work, however, showed that the ratio of calcium to phosphorus did not necessarily determine the action of a diet in producing rickets in dogs, and that if an adequate amount of the necessary "accessory factor" is supplied, the ratio can apparently be varied within wide limits without the appearance of rickets. I think we may now take it as generally accepted that vitamin D has the specific function of regulating absorption of calcium and phosphorus from the gut and deposition as calcium phosphate in bone tissue, particularly at a time when there is a deficiency of either element in the food.

With reference to vitamin D, it was subsequently shown that irradiation of the animals or of their food with ultra-violet rays had the same action as supplying vitamin D by the mouth, and it was assumed that the rays activated a precursor of the vitamin. This assumption was strengthened by the fact that ergosterol, a substance which is known to acquire intensive antirachitic properties on irradiation, has been demonstrated in the skin of animals and in various foodstuffs.

Experiments to determine the cause of rickets in pigs and dogs were carried out by Marek and Wellmann on a fairly large scale. The pigs varied in age from 20 to 123 days, with an average of about 60 days. They were kept in separate sties, well lighted, and under proper hygienic conditions. A variety of foodstuffs were used, and the content in dry matter, protein, calories and minerals, was determined. The rations contained very little vitamin D. Under such conditions rickets was produced if the diet contained too little calcium or too little phosphorus, or too little of both. These authors also attach importance to what they term the "Erdalkali-Alkalizität," a figure which indicates the relative preponderance of the bases CaO and MgO over the acidic P_2O_5. If sufficient absolute amounts of calcium and phosphorus were present, an Erdalkali-Alkalizität of $+25$ was regarded as most advantageous, and ratios too strongly positive in this respect (too much calcium and magnesium), or too strongly negative (too much phosphoric acid) were rachitogenic. Systematic ultra-violet irradiation of the animals over a number of days retarded the disease, but did not prevent it. Ultra-violet irradiation of the food prevented the disease even with a strongly negative Erdalkali-Alkalizität. The same result was obtained by the addition to the diet of vitamin D, cod-liver oil, or pulverised ergot.

The experiments with dogs were also carried out on diets deficient in vitamin D. It was found that a ration deficient in calcium produced rickets, and that this could be prevented by the addition of calcium salts. Rickets was also produced when the amount of lime was increased in the diet of positive Erdalkali-Alkalizität. On the other hand, an increase in the amount of phosphoric oxide in presence of sufficient calcium oxide did not cause rickets, so that a negative Erdalkali-Alkalizität was of less consequence in the case of the dog.

Marek and Wellmann came to the conclusion that the absolute amounts of calcium and phosphorus, and the ratio between them, were of primary importance in the causation or prevention of rickets, since the supply of these two elements

in sufficient amounts and correct proportions prevented rickets even in the absence of adequate amounts of vitamin D, whereas the rachitogenic effect of unsuitable calcium and phosphorus supply could not always be prevented by the addition of vitamin D. As I interpret their conclusions, they would mean that rickets is only conditionally an avitaminosis, that absence of vitamin D only produces the disease when the supply of calcium or phosphorus is incorrect, and that vitamin D is only required when the supply of these two elements is too near the minimum.

In the case of cattle, experimental research into the cause of rickets and osteomalacia was undertaken by myself in conjunction with Dr. H. H. Green and Dr. P. J. du Toit in the course of work designed to clear up the ætiology of the naturally occurring South African disease " stijfsiekte," and to determine the minimum quantities of certain minerals required for health. That work was published under the title " Minimum Mineral Requirements of Cattle," and from the experimental material I subsequently conducted pathological studies of representative skeletons.

The experiments which come under consideration here are those in which heifers received a vitamin-deficient ration containing also insufficient amounts of calcium or phosphorus, or both, but adequate in respect of calories and protein. The animals had free run in a bare paddock exposed to sunlight. Since the daily average of bright sunshine amounted to over eight hours in a clear atmosphere at an altitude of 4,000 feet it can be assumed that there was abundant opportunity for activation of vitamin D precursor, and we therefore need not consider deficiency of vitamin D.

Some of the heifers received a ration containing sufficient calcium, but insufficient phosphorus; some received sufficient phosphorus, but insufficient calcium; some received minimal quantities of both elements, and others adequate quantities of both. In the whole series we had a considerable range of variations, both in regard to absolute amounts and to ratios of minerals. The age of the animals varied from twelve to twenty-two months at the commencement of the experiment, and the period of deficient feeding extended over twenty-five to twenty-seven months. Within this period all the animals receiving inadequate quantities of phosphorus developed typical and extensive lesions of rickets and osteomalacia, but none of the others did so. The results were uniform and clearly showed that deficiency of phosphorus was alone responsible for the disease. Even the two heifers on the very low calcium supply (below 10 g. CaO per day) did not develop the disease, and so showed that the requirements of the growing bovine for calcium are less than for phosphorus.

When examined in respect to Erdalkali-Alkalizität in Marek's sense, the results showed that preponderance of acid over basic ions did not cause the disease, nor did preponderance of basic ions prevent the disease in cases of phosphorus insufficiency. The ratios of calcium to phosphorus laid down for rats by McCollum and co-workers did not apply to our cattle, and we were left with the conclusion

that phosphorus deficiency was practically the only factor we had to consider in the ætiology of bovine rickets and osteomalacia. Similar results have been subsequently obtained with sheep at the same laboratory (Onderstepoort).

The disease we produced artificially on phosphorus-deficient rations proved to be the same clinically and pathologically as that observed in cows and calves running on the veld in certain areas in South Africa, and known as far back as historical records of the subcontinent go. The Dutch called it " stijfsiekte," and the English farmers used the equivalent term " stiff sickness." Before the conclusion of our experimental production of the disease we had become convinced that the naturally occurring disease was a plain aphosphorosis, because it only developed on pastures low in phosphorus, and we could prevent or cure it by any supplements containing phosphorus compounds in assimilable form. Bran rich in phosphorus but poor in calcium was a good preventive, while a calcium supplement containing no phosphorus aggravated the disease.

In the osteomalacia occurring naturally on the veld the first symptom observed is " osteophagia," or bone chewing, a specific form of pica or depraved appetite, known in many parts of the world and already associated with the disease by some of the earliest observers. Apart from its interest as a premonitory symptom of osteomalacia, it should be mentioned that under certain circumstances "bone-chewing " can have grave indirect consequences, by leading to the consumption of carrion infected with *Clostridium botulinum*. The fatal diseases " lamsiekte " of South Africa, " dry bible " and " midland disease " of Australia, and " loin disease " of Texas are all identified as botulism, arising from ingestion of toxic carcase debris by animals addicted to bone chewing. Osteophagia was also displayed by our experimental cattle on phosphorus-deficient rations, but not by the cattle on the calcium-poor ration. The same symptoms may be shown by sheep, and also lead to botulism, but it is usually less pronounced, and seems to appear only in advanced stages of aphosphorosis. Du Toit and Malan observed an " earth hunger " in sheep kept on a low calcium ration, and a similar allotriophagia may be observed in aphosphorosis of cattle when the animals have no access to bones. I regard osteophagia as the discriminating earlier form of a pica, which may become less specific later.

The appearance of osteophagia is associated with a fall in the level of inorganic phosphorus in the blood, and the sinking of this level in grazing cattle is an indication of phosphorus deficiency in the pasture. The South African work showed no such marked depression of the calcium level of the blood in cattle and sheep on calcium-deficient rations, and although low blood-calcium has been reported elsewhere in calcium-starved sheep, it would seem that the calcium level tends to remain more constant than the level of inorganic phosphorus. This sinking of the phosphorus level of the blood is probably the stimulus for the mobilisation of this element in the skeletal reserves and for the resorption of minerals, which leads to atrophy and porosis. Depression of the phosphorus level and incipient osteoporosis could thus be considered as the first stage in

the syndrome we have called aphosphorosis, the final stages of which are rickets and osteomalacia.

Although this hypophosphatæmia is so characteristic of bovine osteomalacia in South Africa, it should be mentioned that the data of Marek and Wellmann for pigs do not show the change so clearly. Their values for inorganic phosphorus varied between low and high in healthy as well as in diseased pigs, but they were able to recognise some relation between the absolute quantities of calcium and of total phosphorus in the blood and the quantities in the diet. In their work they also met the symptom of tetany in eleven out of twenty-seven pigs, *i.e.*, in 40 per cent. of their cases. This symptom does not seem to have been observed in other animals, but has been described in children. In some of the cases of Marek and Wellmann the attacks occurred repeatedly and at short intervals. At the onset of an attack the animal utters a loud cry, the musculature becomes rigid, and rolling of the eyes is noted. The respiration is superficial or arrested, and a cyanotic discoloration occurs on the thinner portion of the skin. After one-half to two minutes the animal recovers. The tetanic spasms are sometimes general and sometimes limited to certain portions of the body, and in some cases these attacks end fatally. Since no such symptoms occur in rickets and osteomalacia in South African cattle, in which blood minerals other than phosphate are more or less normal, but are observed in lactation tetany of European cows, and are then associated with a marked hypomagnesæmia and slight hypocalcæmia, it is of interest to inquire whether the spasmophilia of their rickety pigs was associated with changes in blood minerals. Calcium determinations were carried out on the blood of the killed animals, but were not systematically made during the experiment. The authors state that they could find no definite relationship between tetanic spasms and blood calcium.

In human rickets the level of the blood calcium is very little altered, but the inorganic phosphorus falls just as in the case of cattle and sheep. In children the low phosphorus level can usually be raised by treatment with cod-liver oil, probably because human rickets is generally associated with a D avitaminosis. In scrutinising the various observations we therefore come to the conclusion that, although the main clinical and pathological picture is the same in different species of animals, there are considerable variations in detail. These variations may be in part typical of the species, but are quite probably related to the type of metabolic disturbance which gives rise to the disease.

Although the three factors—vitamin D, calcium and phosphorus—are all necessary for the normal growth of bone, and deficiency of any one of them may theoretically be the cause of rickets, they do not play an identical rôle in ruminants, omnivores and carnivores. In bovines and ovines we have seen that, in presence of sufficient solar radiation, rickets develops under conditions of simple phosphorus deficiency. Although vitamin D may be a significant factor in theory, sunlight was sufficient to prevent rickets on a vitamin-deficient ration in our experiments, so that dietary deficiency of vitamin D does not become a factor in the natural

occurrence of rickets in grazing ruminants, however poor the pasture may be. Our experiments also showed that the requirements of the bovine for calcium are much lower than for phosphorus, and later experiments have proved that the same holds true for the ovine. Under natural conditions cattle and sheep are never likely to encounter a pasture more deficient in calcium than in phosphorus (from the point of view of the physiological requirements of the animal), so that naturally-occurring rickets and osteomalacia in the ruminant will always arise from aphosphorosis. It is, of course, possible that osteomalacia could be experimentally produced in a heavily lactating cow by feeding phosphorus-rich concentrates with a bare minimum of roughage phenomenally low in calcium, but we failed to produce the disease in heifers by this procedure, and such a ration never occurs in practical feeding of dairy cows.

With pigs, however, the position is different. We are not convinced that the Erdalkali-Alkalizität, on which Marek and Wellmann lay so much stress, has the importance they attach to it, or that the ratio of minerals as such, *i.e.*, apart from the absolute quantities which constitute the ratio, has the significance attached to it by some authors. In general practice it is low calcium, with or without vitamin D deficiency, which is the most likely cause of rickets. Pigs are fed on concentrates, which usually contain quite sufficient phosphorus but are poor in calcium, and it is a well-known fact that calcium carbonate and salt are the only supplementary minerals commonly used in pig husbandry.

In the case of the dog the position is not clear, although it would appear that, as in the case of children, vitamin deficiency plays the important rôle. The food of dogs is often poor in vitamin D, and the environment in which they often live may fail to supply the equivalent ultra-violet radiation.

These conclusions regarding the different ætiology of the disease in different classes of animals are supported by the results of preventive and curative treatment of rickets in practice. Rickets and osteomalacia in ruminants are successfully controlled by a supplement of phosphates in the form of bone meal, dicalcium phosphate, or sodium phosphate. So great has been the success of this measure in South Africa in suppressing the ill-effects of aphosphorosis in all its forms that it has revolutionised cattle breeding. Over the greater portion of South Africa, grazing cattle suffer from a form of phosphorus starvation which varies, according to district and season, from slight malnutrition to severe osteomalacia. During the spring, when the young grass is richest in phosphorus, this deficiency may disappear even in bad areas, and the cattle are then able to fill their skeletal reserves against the ensuing dry season, when deficiency becomes acute. They may thus carry through the cycle of their existence, changing from a slight skeletal atrophy at one season to relatively well-stocked reserves at another. But they never have an adequate margin, and when the expenditure becomes heavy, as is the case in pregnancy and particularly during lactation, the latent aphosphorosis, so common on deficient veld, becomes acute, and osteomalacia develops. As protection against the drain, veld cows commonly became sterile in alternate

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seasons. They rarely gave birth to two calves in two successive years, and at lactation their milk yield was unusually low. All this has been changed by phosphorus feeding, and the simple use of a bone meal supplement has rendered cattle rearing profitable in areas in which it was previously unprofitable. The disease "lamsiekte," which, as already pointed out, is botulism, contracted by cattle showing osteophagia, has ceased to be a menace to the farmer. By feeding a phosphorus supplement he removes the osteophagia, and so breaks the ætiological chain of lamsiekte.

In the case of pigs, it is common practice to add chalk or ground limestone to the concentrates, and experience has shown that breeding sows showing fragility of bones and unable to rise can be cured by calcium salts, which do not contain the phosphate ion.

In the case of dogs, cod-liver oil is the recognised cure for the disease, and an outdoor life is known to be an effective preventive measure. In place of cod-liver oil, a variety of commercial preparations containing irradiated ergosterol are sometimes prescribed.

In concluding this section of my discussion, it may be noted that I have omitted all consideration of endocrine disturbances in discussing rickets and osteomalacia of domesticated animals. The influence of internal secretion on calcium metabolism and the formation of bone has been proved experimentally, but so far it has not been possible to demonstrate lesions in the endocrine glands which can be brought into specific relation with rickets and osteomalacia.

I have also omitted the rôle that fluorine is sometimes said to play under certain conditions. This is because there is no convincing histological evidence to show that the lesions of fluorosis are those of osteomalacia, and because the introduction of toxic influences would only obscure the picture I have been trying to present.

Summary.

In summarising the results of my own investigations, and my survey of the literature, I feel justified in stating my conclusions as follows:

(*a*) The existence of rickets and osteomalacia in the strict pathological anatomical sense has been proved in the case of cattle and sheep, and in these species the disease apparently occurs in pure form without complications. (*b*) The disease is also found in pure form in pigs, but is sometimes associated with osteodystrophia fibrosa, a disease which can also appear independently. (*c*) These two diseases also occur in dogs, but rickets seems to be more common than osteodystrophia fibrosa. (*d*) In horses and goats osteodystrophia fibrosa is the common bone disease. (*e*) Although the osteodystrophia malacica (rickets and osteomalacia) of the domesticated animals, as observed in practice, is pathologically the same, it is ætiologically different in different species. In the case of bovines and ovines it is primarily an aphosphorosis, in pigs an acalcicosis, and in dogs an avitaminosis.

(To be concluded.)

Abstracts of Current Literature

On Two Cases of Tuberculosis of the Vulva in the Cow. By F. GMEINER, District Veterinary Surgeon, Vienna. *Wien Tierarztl. Mschr.* 20:349. 1933.

IN the carrying out of diagnostic tuberculin inoculations in Lower Austria two colleagues mentioned diseases of the vulva in cows. Two cases were found which from the pathologic-anatomic standpoint were not merely noticeable, but gave clear signs that a correct diagnosis could be corroborated by a pathologic-anatomical and bacteriological examination. If a correct diagnosis had been made, instead of these cases being treated for a week as being actinomycosis, much time and trouble could have been spared. The cows were on different holdings; their condition and appetite were good, and clinically there was no indication of an internal malady. Both labia of the vulva were converted into hard tumour masses, and infested with numerous transparent, yellowish lumps, and on the upper surface, and especially at the outer edge, were ulcers. Urine was passed normally. An examination per vaginam was impossible. From both cases material from the softened masses was taken under sterile precautions as far as possible, and also from one cow a stalky piece of connective tissue. This material was examined at the laboratory, but actinomycosis could not be found; but on histological examination of the piece of connective tissue typical giant tubercle cells and commencing caseation were discovered, so the material from both cows was submitted to the guinea-pig test. After four weeks the guinea-pigs were killed and post-mortemed, and tuberculosis of the lymph glands was found, and, moreover, the liver and spleen were permeated with numerous yellow tuberculous nodules. In both cases, therefore, tuberculosis was established. In one cow slaughtered tuberculosis of the uterus was not present, but there were a few tuberculous nodules in the lungs. There were miliary, linseed-sized tuberculous nodules in the mucous membrane of the vagina declining in number as they advanced to the portio. Dr. Gmeiner criticises the regulations concerning the reporting of cases of tuberculosis. The law in Austria is that "advanced tuberculosis of the lungs, intestine, uterus, and tuberculosis of the udder" are to be reported. He thinks that "advanced tuberculosis of the genital tract" should be substituted for "tuberculosis of the uterus," and all the more so as tuberculosis of the vulva is easier to recognise than uterus tuberculosis.

The Treatment of Hypoderma Bovis. BAUDET and JE BOER. *Tijdschr. Diergeneesk.*

Because of its easy application in practice, the authors obtained excellent results in the control of hypoderma bovis with the watery extract of derris powder, recommended by Götze in 1932. (1,000 grams of derris powder are drawn

twenty-four hours in 9,000 c.c. water, then a solution of 250 grams of sapo viridis in 1,000 c.c. water is added. The liquid should always be freshly prepared.) In most cases a single washing suffices ; when after a few days a second washing follows, all larvæ are certainly killed. Good results were also obtained with Rotenon as ointment in the concentration of 2 per cent., and with a mixture of Rotenon and Oleum picis in the same concentration. However, on account of the presence of Oleum picis the irritating action of the second mixture on the skin is too strong. A mixture of pix liquida, terebinthina communis, sapo viridis, petrol and spiritus methylatus did not produce the good results expected.

The Ophthalmic Reaction in Brucella Infection of Cattle. By DR. J. VAN HOEDEN. *Tijdschr. Diergeneesk.* v. 60, p. 876. 1933.

THOROUGH examination with a specially prepared antigen has demonstrated that in Brucella infection of cows the ophthalmic test is a sensitive method of diagnosis. This method is independent of the presence of antibodies in the blood serum. Also in animals experimentally infected with living culture the allergic reaction soon became positive. After repeated injections of a killed Brucella suspension the ophthalmic test remained negative, whereas many agglutinins and amboceptors made their appearance in the blood serum. Investigations in infected cattle herds have demonstrated that the allergic ophthalmic test may be considered as a practical method of detecting Brucella infections.

Reviews

Veterinary Hygiene. By R. G. LINTON, Ph.D., M.R.C.V.S. Pp. 471. 129 illustrations and diagrams. Edinburgh : W. Green & Son. Price 21s. net.

PROFESSOR LINTON'S name is so well known as an earnest worker in the cause of veterinary science that any book bearing his name as author is certain to find a ready welcome amongst veterinary and agricultural students and practitioners. In this second edition of his masterly treatise on " Veterinary Hygiene," he has added much in the way of mature judgment and practical experience to his former work. Wisely, too, on special subjects he has called in the kindly assistance of specialists in those matters, and their advice has been generously acknowledged. Veterinary Hygiene has always been of vast importance to the veterinary student, many of whom, coming from our large towns, have never had the opportunity to study the habits of the farm animals under natural conditions; and it is easy to understand that it is not possible to satisfactorily treat them in disease without knowing their normal habits in health. Divided into some six sections, Professor Linton deals with water, its purities and impurities, the vagaries of the weather and their consequences, sanitation, ventilation and air space, building construction, and last, but by no means least, the prevention and control of disease. Fully illustrated and clearly and lucidly described, the second edition of Professor Linton's book has no rival as the text-book for animal husbandry for all the English-speaking veterinary colleges ; and the profession owes him a great deal for all the trouble he has taken to compress in a volume of this size such a fund of useful information.

Practical Animal Husbandry. By WM. C. MILLER, M.R.C.V.S., F.R.S.E., and E. D. S. ROBERTSON, M.R.C.V.S. With a Foreword by Major-General Sir JOHN MOORE, K.C.M.G., C.B., F.R.C.V.S. Pp. 316, with 122 illustrations. Edinburgh: Oliver & Boyd. Price 12*s.* 6*d.*

MESSRS. MILLER AND ROBERTSON have presented the veterinary student, just at the moment when it was most needed, with a compendium of useful practical information condensed into one volume. As expressed by Major-General Sir John Moore in his Foreword: "all the essential factors which have been dealt with by other authors and in other works." There is something else, however, in this work which makes it of especial value as a text-book to the veterinary student. The whole tenor of the book is "practical," and on a perusal of even only a few minutes it becomes palpably evident that the authors are men who not only *know* the subject on which they have written, but are able to explain all about it without unnecessary verbiage. The subjects dealt with include such simple matters as "approaching" and handling horses, cattle, dogs, cats, and all farm animals, not omitting even the farmyard birds, too. Commencing with the ordinary catching and handling, the authors proceed to deal with means of restraint, stable and other vice, conformation, colour, markings, breeds of all kinds; and the subjects of watering and feeding, clothing, grooming, working, shoeing. The fitting of harness and saddlery, a knowledge of which is so important a matter to the townsman student in the present college course, is very carefully considered, and the whole book is so clearly and well written that it must inevitably follow that it will become the recognised text-book for the students of animal husbandry, not only in the veterinary colleges, but also in the agricultural schools. We have every confidence in recommending it as the authorised text-book on, as the title states, "Practical Animal Husbandry," to the students of veterinary schools.

News

THE INTERNATIONAL VETERINARY CONGRESS: SPECIAL PARASITOLOGY COURSES AT MONTREAL.

A course in parasitology for English-speaking veterinary practitioners, lasting for ten days, will commence at the McGill University on August 27th, 1934. The course, which will be practical as well as theoretical, will include the diagnosis, pathology, therapeutics, bionomics and methods of control of all the important parasites of live stock (including dogs and cats), and will occupy about sixty teaching hours. The lectures will be given by Professor Thomas Cameron, M.A., D.Sc., Ph.D., M.R.C.V.S., who formerly held appointments in the London School of Tropical Medicine and Hygiene and in the Edinburgh University. There will be no fee for the course for veterinary surgeons from the British Empire, but a registration fee of $5 will be required from veterinarians from elsewhere. Accommodation (including meals) will be available in the Macdonald College Residence for men at the rate of $8 per week; similar, but separate, accommodation will be available for ladies in the women's residence. Meals will be taken in the common dining room, however. The residences contain gymnasia and swimming pools, and on the campus there is a nine-hole golf course, tennis courts, etc. The College is situated at a convenient distance for excursions to Ottawa and the Laurentian Mountains by road or rail, and to Quebec and other cities on the St. Lawrence by steamer. As the first week-end in September is a national holiday, cheap fares by all these routes will be

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available from Friday night until Tuesday morning. Excursions to various centres of general interest to veterinarians will probably be arranged, including a visit to the Dominion Animal Diseases Research Institute and Experimental Farm at Ottawa. The local railway stations are Canadian Pacific and Canadian National Railways, Ste. Anne de Bellevue; and at the finish of the course, the following steamships will be leaving Montreal for Great Britain: September 7th, 10 a.m., ss. "Letitia" (Cunard Anchor Donaldson) for Glasgow, Belfast and Liverpool; September 7th, 9 a.m., ss. "Duchess of Bedford" (Canadian Pacific) for Glasgow, Belfast and Liverpool; September 7th, 10 a.m., ss. "Aurania" (Cunard) for Plymouth and London; September 8th, 9 a.m., ss. "Montclare" (Canadian Pacific) for Southampton. In addition, the ss. "Empress of Britain" (Canadian Pacific) sails from Quebec on September 1st, at 1.30 p.m., arriving September 6th.

PROVISIONAL TIME-TABLE.

	Morning (Lecture) 9–10 a.m.	Morning (Laboratory) 10.15–12.15	Afternoon (Laboratory) 2–4 p.m.	Evening (Lecture)
(1)	General Introduction	Protozoa	Entomology	Diagnostic technique
(2)	Classification	Flatworms	Roundworms	Laboratory methods
(3)	Pig parasites	Roundworm, Trichinosis	Cysticercosis, etc.	Immunity (1)
(4)	Sheep and Goat parasites	Hookworms, nodular worms, tricho-strongyles, lung worms	Flukes and cestodes	Immunity (2)
(5)	Ox parasites	Piroplasms and trypanosomes	Warbles; cysticcosis and other worms	Therapeutics (1)
(6)	Horse parasites	Sclerostomes and oxyurids	Other worms: Bots	Therapeutics (2)
(7)	Dog and Cat parasites	Ascarids and hook-worms	Liver flukes, tape-worms and Hydatid	Blood parasites
(8)	Poultry parasites	Coccidiosis and blackhead	Tapeworms and roundworms	Parasites
(9)	Fur, Game, etc. parasites	Important parasites of fur animals	Game, fish, etc., in relation to domestic animals	Historical outline of parasitology

ROYAL COLLEGE OF VETERINARY SURGEONS.

A Central Library for Animal Diseases: An Appeal for Financial Support to Augment the Endowment Fund.

Present Scope of the Library.—The Library at 10, Red Lion Square, London, contains a unique collection of literature upon all subjects relating to animals in health and disease. This literature has been gathered during the last 100 years, and comprises books, monographs, periodicals and reports from all parts of the world. Scientific workers may borrow these for reasonable periods or may study in the Library itself. The literary resources which the Library possesses cannot be found to a like extent elsewhere because no other institution possesses so many complete sets of British and foreign veterinary periodicals. The Library was reconstructed and refurnished by

the Council of the Royal College of Veterinary Surgeons in 1927, and formally opened by Colonel L. J. Amery, Secretary of State for the Dominions, in 1928. It is one of the few selected National Libraries whose resources are indexed in the World List of Scientific Periodicals. It acts also as an " outlier " to the National Central Library, and in this capacity its contents are available for students of all branches of science in any part of the British Isles. It has not only been of immense assistance to those engaged in the study and investigation of animal diseases in this country, but scientific workers from overseas are becoming increasingly aware of its value to them and are continually making use of it.

Needs of the Library.—It has become increasingly evident within recent years that the growing needs which the awakening of public interest in animal diseases has created cannot be satisfied by the restricted service which, owing to lack of funds, the Library can at present render. Since the utility and efficiency of a library depends not only upon the value of its resources in books and periodicals, but especially upon skilled library service, it is obvious that the present small endowment fund—the net income from which is less than £80 per annum—will have to be augmented. The Council have supplemented this income by such maintenance grants, never exceeding £100 in any one year, as they have been able to provide from their limited general funds, in addition to small sums they have received from outside sources, notably the Carnegie (U.K.) Trustees. But it is estimated that the maintenance of an efficient library service, including the annual cost of new books, periodicals, binding, etc., and the salary of a qualified whole-time librarian, would require further capital endowment of at least £15,000.

Appeal for Contributions.—The Council, in their desire that the Library should be developed and its public utility extended, have decided to issue this appeal for contributions from those interested in veterinary science, public health and agriculture, as well as from all who have the welfare of animals at heart. They are convinced that should the appeal be successful, the wider and more efficient services which the library could then render would more than justify the increased expenditure, and accordingly ask all who are interested to contribute generously. Contributions, made payable to the Royal College of Veterinary Surgeons, may be sent to the Secretary, 10, Red Lion Square, London, W.C.1.

Publishers' Notices

All communications should be addressed to 7 & 8, Henrietta Street, Covent Garden, London, W.C. 2. Telephone: Temple Bar 8568. Telegrams: "Baillière Phone, London."

Letters for the JOURNAL, literary contributions, reports, notices, books for review, exchanges, new instruments or materials, and all matter for publication (except advertisements) should be addressed to the Editor.

Copy of advertisements should be in the hands of the publishers—Baillière, Tindall and Cox—not later than the 25th of the month, or if proof is required, not later than the 28rd.

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